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1884

NOTES

OF THE LAST FIFTY

LECTURES ON PHYSIOLOGY

GIVEN BY

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FASCICULUS I.

EDINBURGH:
YOUNG J. PENTLAND.
1884.

PREFATORY NOTE.

I have prepared these notes for the assistance of my pupils, at their request. They are intended to serve until the completion of my Text Book of Physiology. Part I. of that work, already published, deals with the subjects of the first twenty-three Lectures. Part II. will treat of Muscle, Nerves, Electricity and the Circulation, and will bring the work up to the beginning of these Notes. I anticipate that it will appear during the present year.

W. RUTHERFORD.

BLOOD.

THE total amount of blood in the human adult is estimated at $\frac{1}{13}$th part of the weight of the body. That would be 13 lbs. of blood in a person weighing 12 stones. In the child at birth the amount is only about $\frac{1}{19}$th part of the weight of the body.

The blood is slightly viscous and also slightly alkaline. Its normal specific gravity is 1055, its normal temperature 100° F. The general composition of human blood in 1000 parts is as follows :—

Water, ...	779·90
Solids of corpuscles, . .	140·10
Serum albumin, } Serum globulin, } . . .	69·40
Fibrinogen, ...	2·20
Extractives and salts, . .	6.80
Fat, ...	1·60
Gases, ...	O, CO_2 & N

About $\frac{1}{3}$ part of the blood consists of corpuscles.

Composition of Red Blood-Corpuscles.

They contain rather more water than solids there being 56·5 parts of water and 43·5 of solids. The solids are almost entirely organic, and

hæmoglobin is far the most abundant. The salts are chiefly potassium chloride and potassium phosphate.

Hæmoglobin is the most complex substance known. Its formula is $C_{600}H_{960}N_{154}FeS_3O_{179}$. Hæmoglobin crystallises. In some animals, *e.g.* the guinea pig, it may crystallise inside the corpuscles. But generally it is necessary to get it outside the corpuscles before it will crystallise. That is generally done by adding water to the blood. The water softens the stroma and allows the hæmoglobin to escape. The stroma may also be softened by adding chloroform or ether.

The crystals have always a red colour, but vary in shape. In the squirrel they belong to the hexagonal system, but to the rhombic system in most other animals. In the human subject they are prismatic. The crystals are very soluble in warm water and also in alkaline solutions. Hæmoglobin behaves like a colloid substance—although it crystallises, it does not dialyse. If we put blood inside a dialyser and add water to break up the corpuscles and allow the hæmoglobin to escape, the hæmoglobin does not diffuse into the water outside. The reason probably is that the molecules of hæmoglobin are too large to pass through the pores of the dialyser. That is the only explanation that has been offered of its not dialysing.

Hæmoglobin exists in two forms, viz., *oxyhæmoglobin* and *reduced hæmoglobin*. The formula for *oxyhæmoglobin* is HbO_2. It forms bright scarlet

crystals. It gives the bright scarlet colour to arterial blood. Oxygen is taken up by hæmoglobin in the lungs and carried to the systemic capillaries, where it is dissociated from the hæmoglobin. That oxygen which is linked to the hæmoglobin in the lungs is spoken of as the respiratory oxygen, in contradistinction to the oxygen which enters into the constitution of the molecule of the hæmoglobin. That molecule never changes. Oxyhæmoglobin is a loose compound. Its respiratory oxygen may be dissociated, by placing the blood in a vacuum, or by exposing it to a substance which is greedy of oxygen, such as ammonium sulphide. *Reduced hæmoglobin* forms crystals of the same shape as oxyhæmoglobin, but of a darker red colour. In arterial blood oxyhæmoglobin alone is present. In ordinary venous blood there is still oxyhæmoglobin present; but there is also reduced hæmoglobin, and the dark red colour of venous blood is almost entirely due to the presence of this reduced hæmoglobin. All the hæmoglobin of ordinary venous blood, however, is not reduced. There is a large quantity of oxyhæmoglobin. But if an animal be deprived of oxygen, in a short time all the oxygen leaves the hæmoglobin, so that it becomes reduced, and the blood is then of a very dark red or purple colour.

The spectrum of blood is the spectrum of its hæmoglobin. When a beam of light is sent through arterial blood much diluted with water, or through a dilute solution of oxyhæmoglobin, and then through

a prism, the HbO_2 produces two dark bands, one in the green, the other in the yellow part of the spectrum. Both absorption bands occur between Frauenhofer's lines D and E. They are named absorption bands, because the substance has absorbed the rays of light at those portions of the spectrum where the bands appear. If the HbO_2 be reduced to Hb, *e.g.*, by adding ammonium sulphide, the green part of the spectrum between the two dark bands produced by HbO_2 disappears, and only one broad dark band remains. But in addition to that there is a darkening towards the red end of the spectrum, which stretches over the line D. If we take ordinary arterial blood and examine its spectrum, it is the spectrum of oxyhæmoglobin. If we take venous blood, its spectrum is the spectrum of oxyhæmoglobin with the green band somewhat darkened. That is to say, reduced hæmoglobin is present, but not in very large amount. The blood of a suffocated animal, however, gives only the spectrum of reduced hæmoglobin. The respiratory oxygen is so loosely combined with hæmoglobin that it is detached by a stream of nitrogen, hydrogen, carbon-dioxide, or nitrous oxide. All these reduce the hæmoglobin without forming any compound with it. The purple appearance of the face of a person who is inhaling nitrous oxide is due to the reduction of the hæmoglobin in the blood generally.

But if a stream of carbonic oxide be sent through

the blood it not only reduces the hæmoglobin, but takes the place of the oxygen. It forms a compound with hæmoglobin, the formula of which is HbCO. It is of a scarlet colour like HbO_2. But the compound HbCO cannot act as a carrier of oxygen from the lungs to the tissues. The CO having taken the place of the oxygen the hæmoglobin can no longer perform its function. Therefore the person who inhales the CO dies from asphyxia. Although that compound is much more stable than HbO_2 it is gradually broken up if artificial respiration be vigorously maintained. But it is generally necessary to resort to transfusion of normal blood.

Hæmoglobin may be split up into many substances, which may be classified in three groups—(1) *Proteids*, (2) *Pigments*, (3) *Acids*. It is especially apt to break up into a proteid, which is an albumin named *globin*, and a pigment named *hæmatin*. That decomposition is effected in the presence of oxygen when the blood is heated, or when caustic alkali, mineral acid, or acetic acid is added to it.

The chief pigments derived from the decomposition of hæmoglobin are the following :—(1) *Hæmatin*; (2) *Hæmin*; (3) *Hæmatoidin*; (4) the *bile pigment*, which is probably the same as hæmatoidin.

Hæmatin ($C_{68}H_{70}N_8FeO_{10}$) is a brown pigment, producible by the artificial means already stated. It forms crystals. It contains all the iron of

hæmoglobin, and can be oxidised and reduced, like hæmoglobin itself.

Hæmin is a hydrochlorate of hæmatin, consisting of one molecule of hæmatin with 2HCl. It is not produced within the body, but derived from hæmoglobin by artificial decomposition. It may be obtained from blood by adding a saturated solution of common salt and glacial acetic acid, and then heating it gently until bubbles begin to appear. The hæmin is produced during the heating, and when the blood cools it crystallises. It forms black crystals. Their production is certain evidence of the presence of blood.

Hæmatoidin ($C_{32}H_{36}N_4O_6$) contains no iron. It has never yet been obtained artificially. It is found in old extravasations of blood. For example, if blood be extravasated in the brain, crystals may be found in it some weeks afterwards. They are mahogany-coloured crystals, somewhat tabular in form. Hæmatoidin is probably identical with the chief pigment of the bile—bilirubin. Bilirubin, like hæmatoidin, produces crystals similar in shape and colour, and when nitric acid is added both substances are oxidised, and the oxidised products give a series of colours beginning with green, apparently showing that the two substances are identical, or very closely allied.

The acids which are derived from the artificial decomposition of hæmoglobin are *butyric acid*, *formic acid*, and others.

The optical characters of the blood depend upon

the shape of the coloured corpuscles, and also upon the state of the hæmoglobin.

1. *Transpareney of the Blood.*—It is transparent only in thin layers. The opacity of a mass of blood is due to the reflection of light from the concave surfaces of the corpuscles. If we take two test tubes, and place a small quantity of blood in each —the same quantity in both cases—and to the one add water, and to the other saturated solution of common salt, the blood + water becomes transparent, while the blood + salt solution remains opaque, although diluted as much as the other. The water renders the corpuscles globular, while the salt solution shrivels them up, and in the latter condition they reflect even more light than they normally do.

2. *The Colour of the Blood.*—It is scarlet in the systemic arteries and in the pulmonary veins ; and it is dark red in the systemic veins and pulmonary artery. The difference in colour has been ascribed to the difference in the shape of the corpuscles. When they are rendered more concave by shrivelling them with saturated solution of salt they reflect more light, and therefore the blood is lighter in colour ; but when they are rendered spherical by the addition of water they reflect less light, and therefore the blood is darker.

The change in the colour of the blood as it occurs in the body is associated with a gaseous change. The brightening of the colour is associated with the entrance of oxygen and loss of

carbon dioxide in the lungs, and the darkening of the colour is associated with the loss of oxygen and entrance of carbon dioxide at the systemic capillaries. A stream of oxygen sent through venous blood arterialises it,—that is, renders it scarlet. A stream of CO_2 sent through arterial blood, renders it dark red. The CO_2 expels oxygen from oxyhæmoglobin. It does not, however, take the place of it, but is linked to sodium salts in the liquor sanguinis. The concavity of the corpuscles is appreciably diminished by a stream of CO_2 if long continued, while oxygen can restore the corpuscles to their former shape. The effect of these gases on the shape of the corpuscles might therefore produce a difference of colour. But if we examine the corpuscles of arterial and those of venous blood under ordinary conditions, no appreciable difference of shape can be detected. The scarlet colour of the blood in the arteries, and the dark red colour of that in the veins must therefore be ascribed mainly, if not entirely, to a difference in the state of the hæmoglobin,—oxygenated in arterial blood, partly reduced in venous blood.

The Liquor Sanguinis or *Blood-Plasma.*—It may be obtained pure by exposing blood to a very low temperature, so near the freezing-point that coagulation is prevented. The corpuscles, being heavier than the blood-plasma, sink, and the plasma is left clear at the top. It is a straw-coloured fluid, of very complex composition. Its

proteids are—(1) serum-albumin, (2) serum-globulin, (3) fibrinogen.

1. *Serum-albumin* is the most abundant proteid. It chemically resembles egg-albumin. There is, however, a slight difference in reaction. Serum-albumin is precipitated by nitric acid, and the precipitate is soluble in excess. The precipitate obtained by adding nitric acid to egg-albumin is not soluble in excess. There is, however, a remarkable physiological difference between them, as proved by the experiment performed by Claude Bernard. He injected egg-albumin into the vein of a dog, and found that it was almost entirely excreted by the kidney. When serum-albumin is injected it is not excreted.

2. *Serum-globulin* (*Paraglobulin* or *Fibrino-plastin*).—This also is found in the liquor sanguinis in considerable amount. The proportion of serum-globulin to serum-albumin is 2 : 3 (Hammarsten) —a much larger quantity than was formerly supposed to exist. It is precipitated by saturating blood-plasma with magnesium sulphate. It yields a white precipitate. The serum-albumin is not precipitated.

3. *Fibrinogen* exists in the blood in far smaller amount than either of the above mentioned proteids. Its proportion is 2·2 parts in 1000. It assumes the form of fine threads—fibrin—when the blood coagulates.

Neutral Fats also exist in the blood, viz., *olein*, *stearin*, and *palmatin*. The amount of fat in the

blood is increased during digestion, and if blood drawn at that time be defibrinated by whipping it with a quill, and then be allowed to stand, the fat rises to the surface and may form a distinct layer, and it may be in so large an amount that when blood is drawn from an animal the fat accumulates on the surface and forms a distinct layer. *Lecithin*, an azotised fat, is present in small amount.

Glucose or *grape sugar* is also present in very small proportion. There is also a *starch-like substance* allied to *glycogen*.

Various effete Organic Solids, viz., Urea, Uric acid, Hippuric acid, Creatin, Creatinin, Xanthin, Hypoxanthin, Indican, all excreted from the blood by the kidneys, and Cholesterin, excreted by the liver.

There is also a trace of yellow pigment of unknown nature in the blood-plasma, and also an aromatic matter, probably consisting of volatile fatty acids. The odour of blood differs in different animals.

Salts of Blood.—The *alkaline salts* are those of sodium and potassium. The sodium salts are the chloride, carbonate, phosphate, and sulphate. The potassium salts are the chloride, phosphate, and sulphate. The *earthy salts* are calcic phosphate, and magnesium phosphate.

The chief salts are *sodium chloride* and *sodium carbonate*. The alkaline reaction of blood is due to alkaline sodium phosphate and potassium phosphate.

The gases of the blood are postponed until respiration is studied.

Coagulation of the Blood.

Coagulation of Milk.—Milk contains a proteid named casein in a state of solution. It can be coagulated by adding rennet to the milk kept at a suitable temperature (100° F.). Rennet contains a ferment—the "milk-curdling" ferment produced in the gastric glands. The whole milk becomes clotted, and after a time the clot contracts and squeezes out a fluid named whey. The clot consists of threads of coagulated casein entangling the milk globules. The whey contains the other constituents of the milk.

Coagulation of Blood.—Blood, after being shed, coagulates in from two to six minutes. Coagulation begins at the surface of contact between the blood and the vessel containing it. The whole blood becomes a jelly, but after a time the clot contracts and expresses a fluid—the serum. The clot consists of threads of fibrin entangling the blood corpuscles. The serum contains the other constituents of the blood. If we examine a piece of the clot with the microscope, the fibrin threads are seen to form a reticulum, enclosing in its meshes the red corpuscles, many of them in *rouleaux*. Most of the white corpuscles are also entangled, but some of those near the surface of the clot emigrate into the serum.

Fibrin may be isolated, by whipping freshly

drawn blood with a quill or brush. When washed for some hours in a stream of water, it is a perfectly colourless stringy substance.

Colour and Shape of Clot.—1. The clot of normal human blood is similar to that of the sheep. As the blood is usually venous, the colour of the clot is dark red throughout, except at the upper surface, where, owing to exposure to the oxygen of the air, the red colour is brighter.

2. In the normal blood of the horse, the upper part of the clot is fawn-coloured, and was formerly named the "buffy coat." The upper surface of the clot is distinctly cupped. The colour and shape of the upper part of the clot is due to *slowness of coagulation* and to the *heaviness of the red corpuscles.* The red corpuscles, being the heaviest part of the blood, always tend to sink in the vessel. When coagulation is rapid, they are entangled by the fibrin threads before they have time to sink. But when—as in horse's blood—coagulation is tardy they have time to settle, so that the upper part of the clot contains fewer of them, and is therefore lighter in colour. The white corpuscles, being of less specific gravity than the red, tend to rise in the blood, and when coagulation is delayed they have time to become decidedly more numerous in the upper part of the clot.

The distinct cupping of the clot of horse's blood results from greater shortening of the fibrin threads in the upper part of the clot, owing to the smaller number of corpuscles in the meshwork.

3. Human blood from a case of inflammation yields a clot resembling that of horse's blood, because coagulation is retarded, and the red corpuscles run more perfectly into *rouleaux*, and so sink more rapidly.

When the blood is kept from coagulating by adding one-third of its volume of a saturated solution of magnesium sulphate, and allowed to stand in a tall narrow glass jar, the red corpuscles sink, and leave a layer of clear plasma above. The white corpuscles rise, and, if they are numerous, they form a distinctly visible thin layer above the red ones.

Theory of Coagulation.—Hewson was the first who supplied some accurate knowledge regarding blood-coagulation (1772). He tied the jugular vein of a horse in two places, excised it, and suspended it vertically (fig. 1). He found that coagulation is delayed for a long time, the corpuscles sink, leaving a stratum of clear liquor sanguinis above. On puncturing the upper part of the vein after the corpuscles had settled, but before coagulation had set in, and drawing off some liquor sanguinis, he found that it coagulated. He therefore proved that coagulation is due to a change in the *Liquor sanguinis.*

Secondly, he proved that coagulation is *not due to a loss of heat*, by rapidly cooling the blood nearly to the freezing-point, and finding that it does not coagulate.

Thirdly, he proved that coagulation is not due

to a loss of vitality, by showing that when a neutral salt such as sodium sulphate is added in sufficient quantity to the blood, coagulation is prevented for an indefinite period, but takes place when the mixture is diluted with water.

Fourthly, Hewson ascribed to the walls of the blood-vessels a power of restraining coagulation,

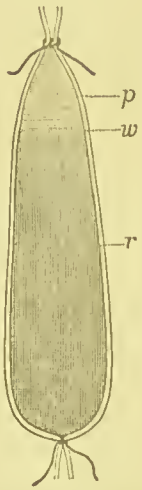


FIG. 1.—Hewson's experiment on blood in vein of horse; *p*, plasma; *w*, white corpuscles; *r*, red corpuscles.

because when blood is left inside a vein it coagulates very slowly, but when poured into a glass it coagulates quickly.

In 1845, Dr Buchanan of Glasgow made important observations on this subject. He was the

first to show that the passage of fibrin from a soluble to an insoluble state is due to the influence of other substances acting upon it under suitable conditions.

He found that when the fluid is drawn from a hydrocele, and poured into say a glass vessel, it does not coagulate spontaneously as blood does. But it is induced to coagulate when the *serum* of clotted blood is added to it. He also found that it coagulates when blood-*clot* is added to it. He washed the clot of blood in a stream of water for several hours to remove the red corpuscles. He then minced the washed clot, dried it, powdered it, and added it to the hydrocele fluid, and it induced coagulation.

He further showed that every part of the blood-clot is not equally efficient. He found the upper more powerful that the lower part of the clot, and that the "buffy coat" of horse's blood is especially powerful in inducing coagulation. With the microscope he observed that white corpuscles are most numerous in the upper part of the clot, and specially numerous in the buffy coat of horse's blood; and, further, that white corpuscles are to be found still clinging to fibrin threads that have been washed. He therefore concluded, *that white blood-corpuscles are the agents which determine the coagulation of fibrin, just as the coagulation of casein is determined by rennet.*

The substance termed "soluble fibrin" by Buchanan is now termed fibrinogen. It belongs

to the globulin group of proteids. It may be obtained from hydrocele fluid by precipitation with an excess of sodium chloride. When rendered solid by that reagent the precipitate is *flocculent*, not fibrous.

Another theory of coagulation was advanced some years ago by Alexander Schmidt. He stated that fibrin does not exist in the blood, but results from the union of two substances—fibrinogen and fibrino-plastin (serum-globulin). Blood contains far more of the latter than is needed to combine with its small amount of fibrinogen when it coagulates,—therefore the serum of clotted blood contains abundance of fibrino-plastin, but no fibrinogen. On the other hand, hydrocele fluid contains fibrinogen, but no fibrino-plastin. Its coagulation when blood-serum is added to it is due—he said—to the addition of the fibrino-plastin needed to combine with the fibrinogen to produce fibrin. Afterwards he discovered that the presence of a ferment is necessary to induce the union of the two substances. He named it *fibrin-ferment*. But Hammarsten has pointed out that the addition of fibrin-ferment only to hydrocele fluid is sufficient to induce coagulation. The presence of fibrino-plastin is not necessary. The fibrinogen of hydrocele fluid is induced to coagulate by the addition of blood-serum, not because it contains fibrino-plastin, but because it contains fibrin-ferment. Schmidt's theory has therefore fallen into the background.

Fibrin-ferment is not present in normal living blood, but it quickly appears when the blood is shed. It seems to arise from some change in the blood-corpuscles, especially the white corpuscles. This ferment may be readily prepared from washed blood-clot, by soaking it in an 8 per cent. solution of sodium chloride. It may also be prepared from defibrinated blood, by pouring it into about twenty times its bulk of alcohol and allowing it to stand for about three weeks. The alcohol coagulates all the proteids. The fluid is then filtered off. The residue is dried, and extracted with water. The aqueous solution contains the ferment. Its nature is unknown.

The ferment can only be obtained from blood that has stood for some time. It cannot be obtained when perfectly fresh blood is run from the blood-vessel of a living animal into alcohol.

Schmidt regarded the white corpuscles as probably the source of the ferment, because he found coagulation most rapid when white corpuscles are most numerous in the blood. That idea is supported by an experiment performed by Lister. He repeated Hewson's experiment (fig. 1), and drew off some liquor sanguinis from the upper part of the vein and placed it in a watch-glass, and it remained for many minutes without coagulating. He then added to the fluid some serum from clotted blood, and he found that coagulation soon took place. He examined the fluid with the microscope, and found little coagula around the corpuscles, especi-

ally around the white ones. He therefore concluded that the white corpuscles are an important cause of coagulation; but as the coagula appeared also, though not to the same extent, around the red corpuscles, these must also be regarded as agents in coagulation.

Lymph, like blood, coagulates spontaneously, especially after it has passed through the lymph glands. It receives in its passage many white and a few young red corpuscles. Before it passes through the glands it coagulates very slowly, apparently because it contains very few corpuscles.

The normal fluid contained in the serous cavities resembles lymph before it has passed through the lymphatic glands. That fluid coagulates spontaneously but very slowly, probably because it contains so few corpuscles. A dropsical effusion into serous cavities, however, has a different relation. For example, if there be a dropsical effusion into the tunica vaginalis it forms a hydrocele. The fluid does not coagulate spontaneously as the normal serous fluid does. It requires the addition of fibrin-ferment. The reason why it does not coagulate spontaneously is either that it contains no corpuscles or so few that they have no appreciable effect.

We are thus just brought back to Buchanan's theory of coagulation, viz., that it is a change induced in a substance which he named "*soluble fibrin*," now named *fibrinogen*, and that the change is due to a ferment produced by blood-corpuscles.

Normally blood does not coagulate in the blood-vessels; but under certain circumstances it does so.

If we insert a needle or thread into a blood-vessel, coagulation takes place around it. Does the needle directly affect the fibrinogen molecules, or does it alter the corpuscles and so lead to the production of fibrin ferment? The latter is probably the case. Hydrocele fluid contains fibrinogen and so is apt to coagulate; yet if we place some in a glass vessel, and introduce a needle into it, no coagulation occurs.

Calcification of the lining membrane of the blood-vessels, which often occurs in old age, tends to cause coagulation of the blood upon it. If the coats of a vessel be injured, as by a ligature, there is a tendency to the occurrence of coagulation at the injured part. Hewson considered that in his experiment (fig. 1) the lining membrane of the vessel prevented the coagulation, since the liquor sanguinis coagulated as soon as it was withdrawn. Lister showed that to be erroneous. He painted a portion of the vein in Hewson's experiment with ammonia externally, and found, that inside the vein, corresponding to the portion painted, coagulation occurred; yet when ammonia is actually injected into the blood it prevents coagulation.

It is the injured lining membrane which here causes the coagulation, as it then acts like a foreign body. The supposed *restraining influence*

of the lining membrane of the vessels, a theory advanced by Hewson and supported by Brücke, is discredited by Lister, who maintains that the vascular lining plays a purely negative part.

In weak states of the system, the blood tends to coagulate in the larger veins, where the blood stream is less rapid. Brücke ascribed the coagulation in such cases to defective vitality of the vascular lining. But it is more likely to be due to the breaking down of the white blood-corpuscles, with production of fibrin ferment.

Styptics, *i.e.*, agents that stop hæmorrhage, *e.g.*, tannin and perchloride of iron, act by coagulating all the proteids in the blood.

Galvanic electricity has a characteristic effect on the blood. A clot forms at both poles, but differing in character from each other. At the negative pole, the clot is loose and hydrogen is given off. At the positive pole, the clot is firm and oxygen is given off. The latter is at once absorbed by the blood. The hydrogen is not quickly absorbed. It produces a froth around the negative pole. In the living vessels it might pass into the capillaries and cause death by thrombosis. Hence, the negative pole is not generally introduced into an aneurism. When electricity is employed to coagulate its contents, the positive pole alone is introduced, and the negative pole is applied to a wet sponge on the skin in the neighbourhood.

When a current of electricity is sent through

defibrinated blood, hydrogen is evolved at the negative pole but no clot appears, oxygen is given off at the positive pole and a slight clot is produced, consisting of coagulated albumen.

Transfusion of Blood.

If much blood be lost, there is great weakness, and the red blood-corpuscles are only slowly reproduced. It is dangerous to introduce any but human blood into the blood-vessels in such cases. It is had recourse to in cases of hæmorrhage and also in cases of carbonic oxide poisoning. It is always dangerous to use any save human blood; *a priori* it might be supposed that the blood of different mammals could be used without injury. It is not so, however; the red corpuscles of the sheep and rabbit quickly break down when added to serum of dog's blood. The red corpuscles of the sheep break down in the serum of human blood, and the stroma of the broken down corpuscles collects and forms emboli, that block up capillaries in various parts of the body.

The blood may be transferred directly from the arm of one person to that of another by introducing a tube into the vein, and having in connection with it an elastic pump, by the elasticity of which blood is drawn from the arm, and by pressure on the pump it is readily transferred into the arm of the other. Or the blood may be collected in a vessel and kept at temperature of the blood (100° F.). When the blood is collected in that way, and

not immediately transferred, it requires to be defibrinated by whipping it with a perfectly clean silver fork, and straining it through muslin, and then injecting it with a syringe into a vein in the arm.

Prevention of the coag of blood: peptone sol
lān ds coag. Tripsin - a ferment of the pancreas,
in glycerine relānds coag. Haycraft and Lal leech
bleeds persistently, and that the blood in the inside
leech remains alum can & remains fluid. The secretion of
(Salivary?) glands of the leech prevent coag; its sol in
1 of Na Cl, has not yet been isolated. Its not a ferment being
affected by boiling. Haycraft injected this into the blood
eels of a dog. Elevated temp of dog: Blood from dog in 3 min
in vitro in vessels not coag. ½ hour after, did not coag.
few pours it's effect entirely passed off, eliminated by the
ney. In the rabbit it did not last as long as in the dog.
The ferment did not succeed so well in the same experiment
haps because he used English leeches instead of German
hes which Haycraft used. Haycraft found that it destroyed
fibrin ferment: to one glass of hydrocele fluid he added serum of
d blood it coag: to another glass he added leech extract
then serum, it did not coag. Hanlaq uses the fibrin
ment. It presents coag in man and animals, but not
stacean blood.
the disease Haemophilia the blood will not coag.
et leeches extract chop up the leeches heads in solution
alt:

RESPIRATION.

The first step towards a real knowledge of the respiration was made by Joseph Black, in 1757, who discovered that during respiration carbon dioxide is added to the air. Black's experiment consists in taking two jars of lime water and driving ordinary air through one and expired air through the other. A turbidity due to calcium carbonate soon appears in the latter.

Lavoisier discovered that carbon dioxide is a compound of carbon and oxygen, and he advanced the theory that the nitrogen of the air is passive while the oxygen enters the blood and combines with carbon. He compared the respiratory process to the combustion of a candle, and he supposed that the lungs are the chief seat of the oxidation. But when it became known that the blood going to the lungs is laden with CO_2 the theory of respiration changed. It is now known that little oxidation takes place in the lungs, its chief seat being in the tissues generally. It also, however, takes place in the blood to some extent.

Respiration essentially consists in an interchange of O and CO_2 between the organism and its surrounding medium. The process may be divided into the *Inner* and the *Outer* Respiration.

The *Inner Respiration* is the gaseous interchange between the blood and the tissues. The *Outer Respiration* is the gaseous interchange between the blood and the air. The latter takes place chiefly in the lungs, and to a slight extent in the skin.

The Pulmonary Apparatus.

The lungs essentially consist of a series of minute cavities, with a dense network of capillaries in their walls. The chest wall with its muscles acts like a pair of bellows for changing the air in the lungs. The air passages consist of the nose, pharynx, larynx, trachea, and bronchi.

The Trachea and Extra-pulmonary Bronchi.

The trachea and extra-pulmonary bronchi have a similar structure. They are kept open by horse-shoe shaped plates of hyaline cartilage that partially surround the trachea and bronchi at short intervals. The cartilage plates are deficient posteriorly opposite the œsophagus, the space being filled up with muscle. The cartilage plates are embedded in strong fibrous membrane, extensible and elastic, so that when the larynx is drawn up in the act of swallowing, the trachea is readily elongated, and recoils to its former length when deglutition is over.

The trachealis muscle is found at the posterior part of the trachea and extra-pulmonary bronchi, where the cartilage plates are deficient. It con-

sists of non-striped fibres, which are mostly transverse in their arrangement. The fibres pass between the ends of the cartilage rings, and to a slight extent upon their inner surface.

They are also found in the spaces between the ends of the rings, so that the muscle forms a continuous layer from above downwards. There are also some longitudinal bundles of muscular fibre at the posterior aspect of the trachea, outside the transverse fibres, and passing from the end of one cartilage to another at a variable distance along the trachea. The muscle is supplied by the recurrent laryngeal branch of the pneumogastric nerve, on the course of which there are many small ganglia.

The mucous coat consists from within outwards of—

(*a*) Ciliated epithelium—stratified.

(*b*) A membrana propria of endothelium, viz., Débove's membrane.

(*c*) A membrana propria, composed of a clear, apparently homogeneous, material.

(*d*) Connective tissue in two layers,—viz., areolar tissue with some adenoid tissue, and outside that a layer of longitudinal elastic fibres.

The submucous coat consists of loose areolar tissue, with somewhat large vessels and small mucous glands. Externally, the submucous coat merges into the fibrous membrane enclosing the cartilage.

Mucous glands are numerous in the trachea and

bronchi. They are compound glands, largest at posterior part of trachea, where their sacs lie outside the trachealis muscle, their long ducts piercing the muscle. Smaller glands occur inside the cartilages, their sacs being in the submucous tissue. The ducts are lined with ciliated cells, the secreting part of the gland—with mucin-forming cells.

Intra-pulmonary Bronchi.

Within the lung the bronchi repeatedly divide in a manner mostly but not always dichotomous. The smallest bronchi, viz., the *bronchioles*, open into clusters of air vesicles.

Structure of Intra-pulmonary Bronchi, excepting the Bronchioles.

Externally, there is a sheath of loose areolar tissue, containing plates of hyaline cartilage at intervals. The plates are not ring-like as in the trachea, but irregular in shape, and not confined to any special part of the circumference of the bronchus. Usually three plates may be seen in a transverse section (fig. 2, *c*).

The mucous membrane consists of—

(*a*) Ciliated epithelium—stratified.

(*b*) Débove's membrane.

(*c*) Homogeneous basement membrane, present in human trachea and bronchi, but not present in lower animals.

(*d*) Areolar tissue with longitudinal bundles of elastic fibres, that give rise to thickenings of the mucous membrane.

(*e*) A layer of non-striped muscles arranged in a circular manner.

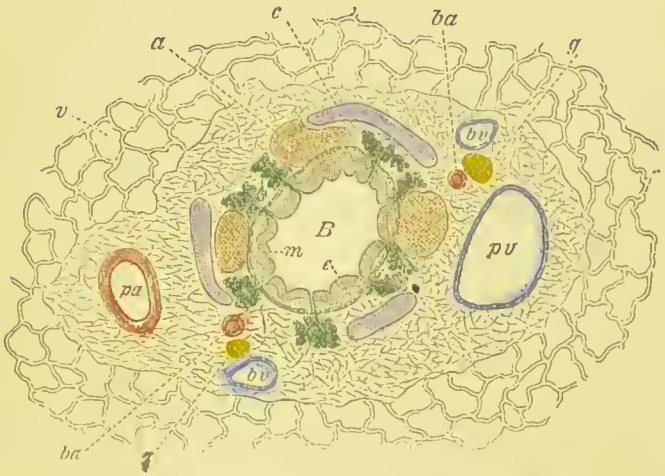


FIG. 2.—Transverse section of an intra-pulmonary bronchus. *B*, Cavity of bronchus ; *pa*, pulmonary artery ; *pv*, pulmonary vein ; *ba*, bronchial artery ; *bv*, bronchial vein ; *g*, nerve with ganglion ; *C*, Cartilage ; *e*, epithelium ; *m*, bronchial muscle ; *a*, mass of lymph follicular tissue. The bronchial glands are seen piercing the muscle and opening internally. The air vesicles of the surrounding lung tissue are seen externally.

The submucous tissue consists of ordinary areolar and adenoid tissue. The latter is mostly collected into cord-like masses—the lymph-follicular cords of Klein (fig. 2, *a*).

Mucous glands are numerous. Their sacs are placed in the submucous tissue, within the carti-

lage plates or between their ends. Their ducts pierce the muscular coat and mucous membrane. The glands, no doubt, are under the influence of nerves. They may be excited by various agents, *e.g.*, ammonium benzoate, ipecacuan, senega.

Blood-vessels.—Each bronchus is accompanied by a branch of the pulmonary artery and pulmonary vein, usually placed on opposite sides of the bronchus (fig. 2, *pa*, *pv*). There are mostly two branches of the bronchial artery with accompanying veins (*ba*, *bv*), each artery and vein forming a pair on opposite sides of bronchus.

Nerves.—A nerve trunk with ganglia upon it runs alongside each pair of bronchial vessels (*g*).

Fat cells occur in the bronchial sheath near the blood-vessels.

The Bronchioles.—The epithelial cells lose their cilia, so that near to the terminations of the bronchioles in the air vesicles there is only a single layer of cubical non-ciliated cells on Débove's membrane. There is no homogeneous basement membrane, no mucous glands, no cartilage. The muscular fibres form a well-marked layer. Outside the muscle there are networks of elastic fibres continuous with those in walls of adjacent air cells.

General Substance of the Lung.

Lobules.—The lobes of the lung consist of a large number of lobules. By some authors the term lobule is applied to the clusters of air vesicles into which a bronchiole opens. But it is more accurate

to regard the lobules as portions of lung tissue mapped out by white lines of fibrous tissue—named the *interlobular septa* The lobules included in these septa are variable in composition, shape, and size. They are, however, always visible to the unaided eye.

The interlobular septa consist of fibrous tissue continuous with the fibrous sheaths of the bronchi and the subpleural fibrous tissue at the surface of the lung. The septa contain some smooth muscle, and many lymphatics and blood-vessels.

Infundibula.—Within the lobules the bronchiole ends in several *lobular, alveolar,* or *infundibular passages.* Each passage is an irregular channel surrounded on all sides by alveoli or air cells. An alveolar passage with its cluster of air cells is named an infundibulum. There are several infundibula in connection with each bronchiole. Rindfleisch uses the term *acinus* to designate the group of infundibula in relation to a bronchiole, while some authors use the term lobule in the same sense. The former term is scarcely necessary. The latter is misleading. The muscular fibres and cubical epithelium of the bronchiole are continued into the alveolar passages, and are found at the divisions of the passages, but not in the walls of the air cells.

The alveoli or air cells are about 250μ or $\frac{1}{100}$ inch in diameter. They are rounded, oval, or hemispherical, and surround the alveolar passages. The wall of the air cells consists of a thin vascular

membrane, the *alveolar membrane* composed of epithelium, connective tissue, capillaries, and lymphatics.

The epithelium of the alveolar membrane consists of (1) large, clear, polygonal scales, some nucleated, others without nuclei; (2) small granular nucleated cells occurring here and there between the large plates. These may occur singly or in clusters of two or more.

Minute openings termed *osteoles* or *pseudo stomata* (Klein) occur here and there between the large squames. They lead into the lymph spaces of the alveolar connective tissue, and foreign particles may enter the lymphatics through them.

The connective tissue of the alveolar membrane contains many networks of elastic fibres.

These fibres recoil and so aid expiration. There is also some ordinary connective tissue with a matrix, homogeneous or fibrillated, containing connective tissue corpuscles.

The capillaries of the alveolar membrane form a dense network, and thus give a large surface for exposing the blood to the air. Most are covered only by alveolar epithelium, some are embedded in the connective tissue (fig. 3).

Blood-vessels of the Lung.

The branches of the *pulmonary artery* and *vein* accompany the bronchi. The branches of the pulmonary artery do not anastomose with one another; those of the pulmonary vein do. These

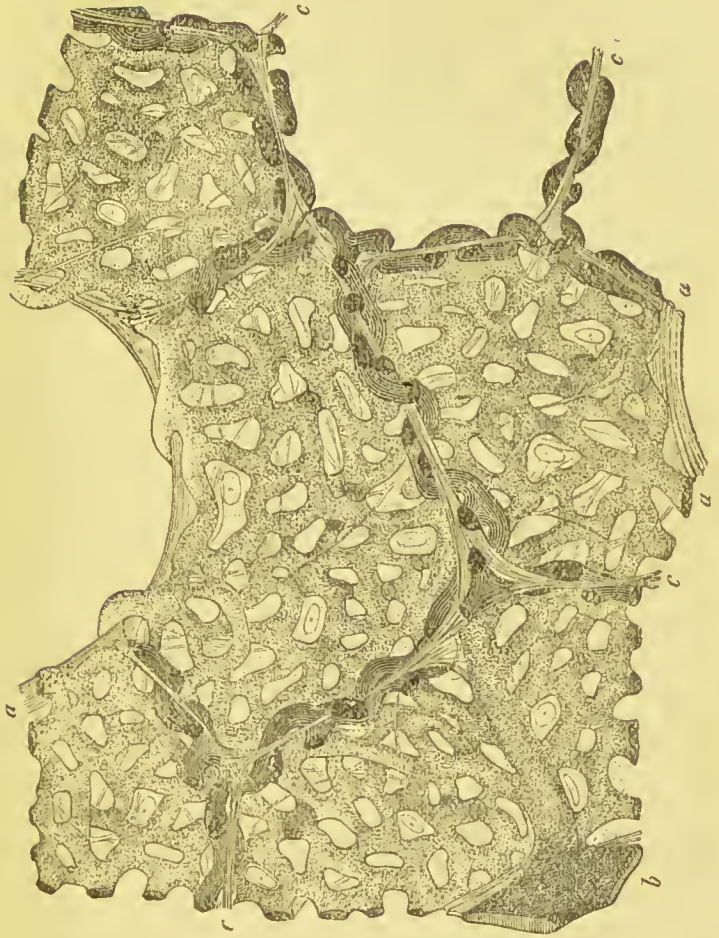


FIG. 3.—Alveolar capillaries of human lung injected. *b*, small branch of pulmonary artery; *aa*, free margin of alveoli; *cc*, alveolar membrane seen in profile. × about 100 diam. (Schulze).

branches are continued down to the infundibula, where they open into the alveolar capillaries.

The bronchial arteries and veins accompany the bronchi. The arteries convey arterial blood to the capillaries of the bronchi, bronchioles, interlobular septa, and pleura. Most of the blood of the bronchial arteries returns from the lung in the bronchial veins, but a part of it is returned by the pulmonary veins. The capillaries of the bronchioles, which receive blood from the bronchial artery, anastomose with the pulmonary artery capillaries in the neighbouring alveoli. The alveolar membrane is nourished by the blood of the pulmonary artery.

Lymphatic System of the Lung.

The *pleura* is closely related to the lymphatic system of the lung. The pleural cavity is a large lymph sac. It consists of two layers, *parietal* and *visceral*. The parietal layer lines the wall of the chest, the visceral layer covers the lung, and the two layers are continuous at the root of the lung and below it. The superficial layer of the pleura, *the pleura proper*, is composed of a dense fibrous tissue covered by a layer of endothelium. The *deep layer* is composed of a loose areolar tissue, which in the case of the pleura pulmonalis is continuous with the interlobular septa. The cavity of the pleura directly communicates with lymphatics by minute openings named stomata. These openings are bounded by cells, and they are found

both in the pleura pulmonalis and the pleura costalis.

The pleural lymphatics form a network in the deeper layer of the pleura. They communicate with the pleural cavity through the above mentioned stomata. They are also the lymphatics of the alveolar walls at the surface of the lung. Their lymph passes to the lymphatics of the interlobular septa, and through these into the peribronchial lymphatics.

The alveolar lymphatics begin in the cell spaces in the connective tissue of the alveolar membrane, and pour their lymph into the peribronchial lymphatics.

The bronchial lymphatics take origin in the cell spaces of the mucous and submucous connective tissue of the bronchi. The lymph passes from them to the *peribronchial lymphatics*, outside the cartilages of the bronchi, by which it is conveyed to the bronchial lymph glands at root of lung.

The collapse of the lung during the act of expiration promotes the flow of lymph through these lymphatics out of the lungs. During the act of inspiration there is a tendency of the lymph to return, but it is prevented from so doing by numerous valves in the lymphatics, which are similar to the valves of veins.

The lymphatics of the lung have been injected in the living dog and rabbit, by injecting into the trachea a fluid containing fine particles of vermilion. It finds its way down the bronchi and

gets into the alveoli. The solid particles pass through the osteoles into the alveolar lymphatics, from which they pass into the lymphatics of the lung generally. Particles of inhaled carbon find their way into the alveolar lymphatics in a similar manner.

Probably they are drawn into the lymphatics through the osteoles during the act of inspiration, because at that moment the alveoli are enlarged, and the alveolar membrane therefore stretched (Klein).

Nerves of the Lung.

The lungs are supplied by the *vagus* and *sympathetic* nerves. Branches from these nerves form the anterior and posterior pulmonary plexus at the root of the lung, from which numerous branches pass along the bronchi, each bronchus having two nerve trunks near the bronchial artery and vein. There are many ganglia on them. The sympathetic is motor for the blood-vessels; the vagus is motor for the bronchial muscles, and sensory for the mucous membrane of the bronchi and for the lung generally. It is not known whether the nerves are secretory to the bronchial glands. Regarding the functions of the ganglia nothing is known. Are they reflex centres for mucous membrane, bronchial muscles, or blood-vessels? They may be compared to the ganglia in the intestinal wall, which are reflex centres for the glands and muscular fibres there.

The great function of the lung is the aeration of the blood. The mucus discharged into the bronchi gives moisture to the air, and entangles solid particles. The cilia of the epithelium lash upwards, and move the mucus into, and up through, the trachea to the pharynx, where it is swallowed.

The functions of the bronchial muscles are more difficult to understand. It has been suggested that the bronchial muscles may contract peristaltically, and so assist in moving the mucus out of the lung. That cannot be the action of the trachealis muscle, nor is it likely to be the function of the muscular fibres of the bronchioles, nor of those around the alveolar passages, for there are no mucous glands in these parts.

The muscular fibres in the interlobular septa, and the layer of smooth muscle found in the deeper part of the pleura in the guinea pig, cannot have anything to do with the expulsion of the mucus.

Laudois has suggested that the tracheal and bronchial muscles probably resist over-distension of the trachea, bronchi, and alveolar passages, and he supposes that they are thrown into activity during forced expiration, *e.g.*, during blowing, singing, and perhaps during speaking.

Mechanism of Respiration.

The air in the lungs is renewed at short intervals by a bellows action of the chest. If the

chest wall is removed from—say a dead rabbit, the animal suspended by the head, the trachea divided and a cannula with small lateral opening for escape of air tied in its lower end, and an elastic pump connected with the cannula,—the respiratory movement of the lung may be imitated. The lungs expand in all directions when the air is driven into them. When the inflation is over, the lungs collapse, owing to recoil of the stretched elastic tissue around the air vesicles. Within the chest, the elastic tissue of the lung aids in expelling the air; but no complete collapse occurs unless an opening be made into the pleural cavity. The collapse which ensues is due to elastic recoil of the lung, and not at all to the pressure of the air admitted into the pleural cavity.

With the chest in its normal condition, air is *drawn* into the lungs by contraction of diaphragm and elevation of the ribs. The action of the diaphragm may be illustrated by a model (fig. 4), consisting of a glass jar, closed below by an india-rubber membrane, to represent the diaphragm; and closed above by a cork holding a glass tube, representing the trachea, with a bladder tied upon its lower end to represent an air vesicle.

The bladder is inflated, and the cork then pushed firmly in. That represents the state of inspiration —the diaphragm being flattened, and the air vesicle distended. When the elastic membrane

is pushed inwards (A), the air vesicle collapses (B). When the elasticity of the membrane is allowed to flatten it, air is drawn in through the tube, and the air vesicle expands. The *elasticity* of the artificial diaphragm in the model plays the part of the *contractility* of the living diaphragm.

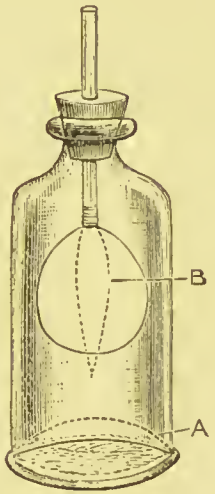


FIG. 4.—Glass jar model to show action of diaphragm and air vesicle.

During inspiration, the cavity of the chest is enlarged from above downwards, by the descent of diaphragm. It is also enlarged from side to side by the elevation of the ribs, and from before backwards by the elevation of the ribs and sternum. The respiratory movements are therefore *diaphragmatic* and *costal*.

Ordinary Respiration.

Ordinary respiration is both diaphragmatic and costal.

Ordinary Inspiration.—The diaphragm contracts and becomes somewhat flattened. The ribs are raised. The upper rib and upper end of sternum are almost motionless during ordinary respiration. But all the ribs below the first—rise.

The mobility of the ribs increases from above downwards. The ribs are arcs of circles, that increase from above downwards. They rotate around axes passing from their posterior extremities to the costal cartilages. They slant downwards and forwards, so that when raised they lift the sternum forwards and upwards.

The ribs are elevated by—

(*a*) The *levatores costarum* muscles of the back passing downwards from the traverse processes of the vertebræ to the ribs.

(*b*) The *external intercostal muscles* extend from the necks of the ribs forward to the costal cartilages. Their fibres are directed downwards and forwards.

(*c*) The *internal intercostal muscles* extend from the sternum to the angles of the ribs. Their fibres are directed downwards and backwards.

All are agreed that the external intercostals elevate the ribs. When exposed in the chest of an animal they can be seen to contract at inspiration.

The action of the internal intercostal is disputed. The portion between the costal cartilages certainly raises the ribs. When exposed in a living dog, it can without difficulty be seen to contract, especially when inspiration becomes somewhat exaggerated in dyspnœa. But it is difficult to say when the interosseous parts of the internal intercostals contract. Even when exposed in a living dog by removing the external intercostal it is difficult to say when the fibres contract.

Haller and others have maintained, on theoretical grounds, that the whole of the internal intercostal elevates the ribs ; while Hutchinson and others have argued that the interosseous part of the muscle lowers the ribs, while the intercartilaginous part raises them.

The latter view has been supported by the use of elastic bands acting on a pair of parallel wooden bars, intended to represent the ribs. The model was devised by Bernoulli, and has long been in use. But it is entirely misleading. Each rib is the arc of a circle that moves in a way entirely different from the bars of Bernoulli's model.

If we take the skeleton of a human chest with the ribs and cartilages movable, fix nails at intervals in the ribs, and stretch elastic bands from one rib to another, so as to imitate the fibres of the external intercostal at one time (fig. 5), and those of the interosseous part of the internal intercostal at another (fig. 6), the ribs are elevated by both

arrangements. In both cases, the lower ribs being arcs of greater circles, and more movable than the upper ribs, are elevated. Therefore the shortening of the interosseous internal intercostal fibres certainly can elevate the ribs. If the lower ribs be held by the hand, so that they cannot move, the upper ribs are drawn down by the bands arranged

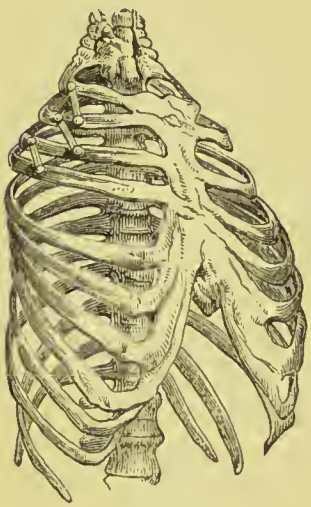


FIG. 5.—Human chest-wall, showing action of external intercostal muscles imitated by elastic bands. (From a photograph.)

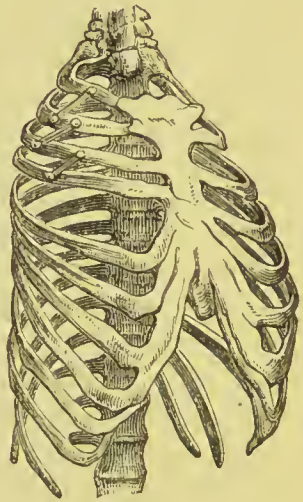


FIG. 6.—The same showing effect of elastic bands arranged as interosseous fibres of internal intercostal muscle.

either as the external or as the internal intercostal. But the ribs cannot be pulled down by the bands arranged as interosseous internal intercostal fibres, unless the lower ribs are firmly held; therefore, those who support the idea that the interosseous internal

intercostal fibres depress the ribs in ordinary expiration, require to show that during ordinary expiration the lowest ribs are forcibly pulled down. There is no evidence of any such action in ordinary expiration. The whole internal intercostal is probably a muscle of inspiration. But the action of the muscle can only be determined by experiment, and, as already stated, the results of experiments are not conclusive.

Ordinary expiration is effected by—

(*a*) Weight of chest wall.

(*b*) Elasticity of lungs.

(*c*) Elasticity of costal cartilages twisted during inspiration.

(*d*) Elasticity of abdominal wall.

The ascent of the diaphragm during ordinary expiration results from the elasticity of the lungs and that of the abdominal wall. There is no evidence that any muscles are concerned in ordinary expiration. There is no sense of muscular effort. Inspiration is purely muscular, ordinary expiration is probably non-muscular. There is a sense of relief from effort, the moment inspiration ends.

Respiratory Movements of Glottis and Nostrils.—The glottis is opened at each inspiration to allow the air to readily enter the trachea. It is opened by the posterior crico-arytenoid muscles rotating the arytenoid cartilages around a vertical axis, so as to turn their anterior margins outwards, and with them the vocal cords forming the lips of the glottis. The nostrils dilate during forced inspiration, and

in some persons they also dilate during ordinary inspiration.

Forced Respiration.

Forced Inspiration.—All muscles able directly or indirectly elevate the ribs—contract.

Auxiliary Muscles of Inspiration.—The lower jaw is fixed to enable muscles attached to it to draw up the hyoid bone.

The hyoid bone is elevated by	Genio-hyoid. Mylo-hyoid. Stylo-hyoid. Digastric.
The sternum is elevated by	Sterno-hyoid. Sterno-thyroid. Thyro-hyoid. Sterno-mastoid.
The upper ribs are elevated by	Scaleni. Cervicalis ascendens. Serratus posticus superior
The shoulder bones are elevated and pulled backwards by	Trapezius. Levator anguli scapulæ. Rhomboideus major. ,, minor.
The ribs are drawn up to the elevated shoulder bones by	Serratus magnus. Pectoralis major. ,, minor. Subclavius.

Forced Expiration.

The abdominal viscera are pushed up against diaphragm by	Obliquus externus. ,, internus. Transversalis abdominis. Levator ani.

The ribs are depressed by
- Rectus abdominis.
- Longissimus dorsi.
- Quadratus lumborum.
- Serratus posticus inferior.
- Triangularis sterni.

The muscles of forced expiration are more powerful than those of forced inspiration. That may be shown with a mercurial manometer. The tube connected with the manometer should be placed in the nostril to avoid any suction by the mouth. It is, however, more convenient to place the tube in the mouth, and with a little care suction may be avoided. A forced expiration can support from three to four inches of mercury. A forced inspiration is only about half as powerful.

The respiratory movements differ in the two sexes in the adult, and also differ with age. In the adult male the diaphragm is more used than in the female. In the female the ribs are more used than in the male; therefore the respiratory movement is but little interfered with in the condition of pregnancy.

In children of either sex, during the first three years the respiration is chiefly diaphragmatic.

The Respiratory Rhythm.—The respiratory movements may be registered by the stethograph of Marey (fig. 7). It consists of a tambour with a tube (*t*) passing from it to a tambour lever placed against a blackened cylinder. The instrument is placed on the chest, and tied round the back with a tape. The bar resting on the chest has a spring

(*s*), which is bent when the chest expands, and recoils during expiration. The movements of the spring are transferred to the air in the tambour by a toothed rod (*a*) fitting into the toothed extremity of a bar (*b*) jointed to a metallic plate fixed to the elastic membrane of the tambour. Fig. 8 shows a tracing taken in the above manner from a chest with normal breathing. The curve traced by the lever falls during inspiration, rises rapidly during

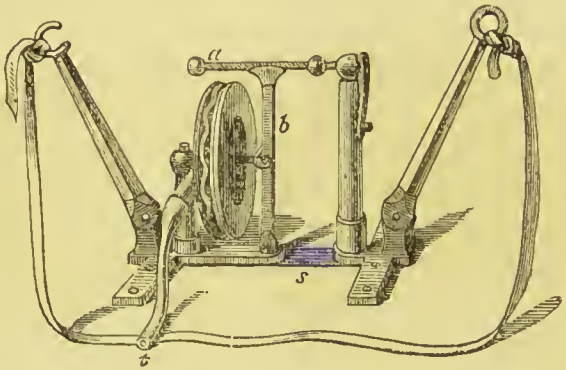


FIG. 7.—Stethograph of Marey.

the first part of expiration, and very slowly towards the end of expiration. It is convenient in practical medicine to regard the last part of the expiratory movement as a *pause*. There is in normal breathing usually no pause, but the movement at the close of expiration is so slight that it can scarcely be seen, unless a recording apparatus is used. If we take the rhythm as having no pause, which is usually the case, the length of the inspiratory is to that of the expiratory move-

ment as 3 to 7. But if we regard the closing part of expiration as virtually a pause, the rhythm is inspiration as 3, expiration as 4, and the pause as 3. These numbers, however, are not invariable, as may be seen by comparing the ordinates in fig. 8 with the millimeter scale drawn below it.

Respiratory Sounds.—An audible sound is produced, both at inspiration and expiration, by the friction of the air in the air passages and air vesicles. The sound may be distinguished into

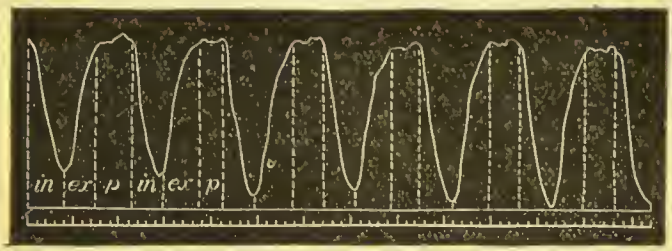


FIG. 8.—The normal respiratory movements recorded by the stethograph. *in*, inspiration; *ex*, expiration; *p*, pause. The scale drawn below indicates millimeters.

three parts, according to its character. (1) *The tracheal sound*, heard over the trachea; a blowing sound somewhat harsh in character. (2) *The bronchial sound*, heard over the bronchi; also a blowing sound harsh in character, not quite so high in pitch as the tracheal sound. (3) *The vesicular sound*, a faint rustling sound due to the movement of the air in the lobular passages and alveoli, and best heard over the apex and base of the lung where there are no large bronchi.

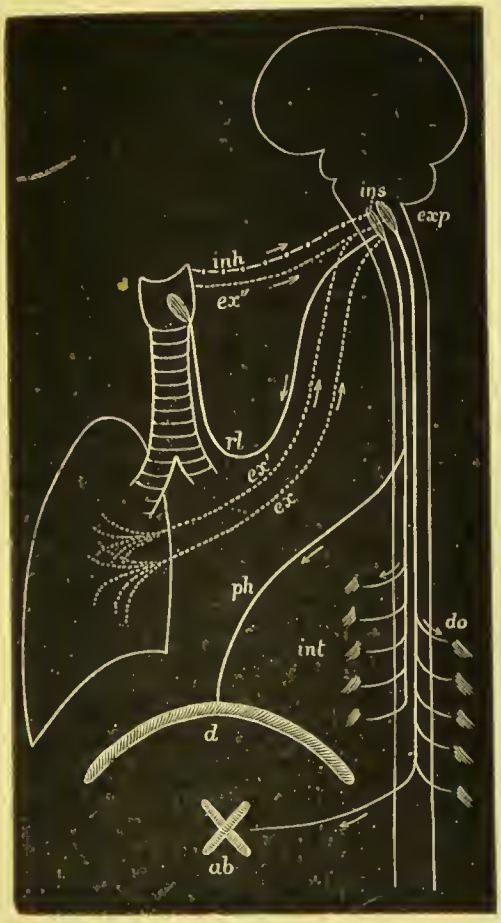
The inspiratory is louder and longer than the expiratory sound, because the movement of expiration produces an audible sound only at its commencement. The relative duration varies somewhat. Taking the inspiratory sound as 3, the expiratory sound may be 2, or even so short as 1, that is, only a third of the length of the inspiratory sound.

Nerve Mechanism of Respiration.

The nerve centre is placed in the medulla oblongata, at or near the root of the pneumogastric nerve. It extends along the floor of the fourth ventricle, from just above the root of the vagus, down nearly to the point of the calamus scriptorius.

The position of the centre has been ascertained by experiment. The whole brain may be removed down nearly to the root of the vagus, and the respiration continues unimpaired. But when the slicing is continued downwards to the point of the calamus scriptorius, respiration ceases.

The respiratory centre is bilateral. A vertical section in the middle line isolates the halves. Destruction of one-half of the medulla produces paralysis of the respiratory muscles of the same side. There is a bilateral inspiratory and a bilateral expiratory centre. The similar centres on both sides are so co-ordinated that they act simultaneously as one centre.



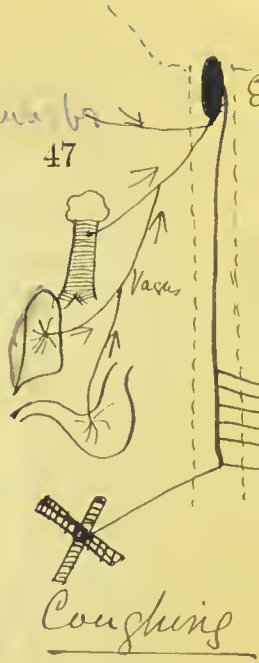


FIG. 9.—Scheme of the chief respiratory nerves. *ins*, inspiratory centre; *exp*, expiratory centre. Motor nerves are in smooth lines. Expiratory motor nerves to abdominal muscles, *ab*; to muscles of back, *do*. Inspiratory motor nerves; *ph*, phrenic to diaphragm *d*; *int*, intercostal nerves, and *rl*, recurrent laryngeal to larynx; *ex*, pulmonary fibres of vagus that excite inspiratory centre; *ex′*, pulmonary fibres that excite expiratory centre; *ex″*, fibres of superior laryngeal nerves that excite expiratory centre; *inh*, fibres of superior laryngeal that inhibit inspiratory centre.

The motor nerves of *ordinary inspiration* are the—

Phrenic nerves to diaphragm.

Intercostal nerves.

Inferior laryngeal nerves to the crico-arytenoid muscles that open the glottis.

The motor nerves of the *auxiliary muscles of inspiration* are the—

Cervical and upper dorsal nerves to various muscles of neck and upper part of chest.

The spinal accessory nerve to the sterno-mastoid and trapezius.

The ninth nerve to the genio-hyoid, sterno-hyoid, thyro-hyoid, and sterno-thyroid muscles.

The fifth nerve to the mylo-hyoid and anterior belly of digastric.

The seventh nerve to the stylo-hyoid, and posterior belly of digastric.

The motor nerves of expiration are the lumbar and sacral nerves supplying the muscles of the abdomen, and those at the lower part of back.

Effects of Lesions of the Motor Nerve Apparatus.—1. Division of spinal cord just below the origin of the phrenic nerves paralyses all the expiratory muscles, and also the intercostals. The diaphragm not being paralysed, the respiration continues.

2. Section of one phrenic nerve paralyses one-half of the diaphragm. Section of both phrenics

completely paralyses the diaphragm. Inspiration is continued by the intercostals and the auxiliary muscles, but the respiration is laboured.

3. Division of the spinal cord above the origin of the phrenic nerves is followed by death, owing to paralysis of diaphragm and intercostal muscles.

The respiratory movements are usually involuntary. Their exciting cause is referable to the state of the blood.

Proof.—If a pair of bellows be connected with the trachea, and artificial respiration performed rapidly, the blood becomes hyperoxygenated, and on stopping the bellows movement the animal does not resume breathing until the excess of oxygen in the blood is used up. This condition of no breathing because of excess of oxygen in the blood is termed *Apnœa.*

On the other hand, when an animal, *e.g.*, a rabbit, is placed in a confined atmosphere, say under a bell jar, the respiration becomes exaggerated; that is the condition of *Hyperpnœa.* The respiratory movements then become still more exaggerated and at the same time laboured; that is the condition of *Dyspnœa.* And unless fresh air is admitted suffocation or *Asphyxia* ensues.

The exaggerated breathing in hyperpnœa and dyspnœa is chiefly due to the deficiency of oxygen in the blood, and also—though to a far less extent—to the accumulation of CO_2, as may be proved by the following experiments:—

Experiment 1.—If an animal breathe nitrogen,

the oxygen of the blood soon becomes deficient, but CO_2 does not accumulate. Dyspnœa rapidly supervenes.

Experiment 2.—When an animal breathes a mixture of CO_2 and O, with the CO_2 so abundant that CO_2 must accumulate in the blood, but with the O so abundant that the blood is thoroughly oxygenated,—the accumulation of CO_2 renders the animal drowsy, as if narcotized, and produces some hyperpnœa, but not nearly so rapidly nor to so marked an extent as happens when oxygen becomes deficient in the blood. Therefore the inspiratory centre is more excited by deficiency of O than by accumulation of CO_2.

The deficiency of oxygen has a direct influence on the medulla. That has been proved by cutting away the brain above the medulla, dividing the spinal cord below the phrenic nerves, and dividing all the nerves connected with the medulla and cervical part of spinal cord, except the phrenics, so that no afferent nerves can influence the respiratory centre. Deficient oxygenation of the blood under those circumstances produces dyspnœa. In that case the stimulation of the inspiratory centre must be direct, because the phrenics, being the only nerves left undivided, are *efferent* nerves.

The excited breathing is doubtless owing to deficiency of oxygen in the respiratory centre itself, dependent on its deficiency in the blood.

In the experiment just described the periodic discharges from the inspiratory centre must be

due either (1) to automatic discharge of energy from the cells of the centre, similar to the periodic discharges from the ganglia of the heart; or (2) to stimulation of the cells by some chemical condition of the lymph which pervades them.

The first explanation seems the more probable of the two. Perhaps the cell protoplasm has a peculiar relation to oxygen, a deficiency of oxygen leading to more rapid discharges from the cells, an excess of oxygen retarding, or for a time even arresting the discharges. Pflüger, however, prefers the second theory above stated. He supposes that the inspiratory centre is constantly excited to periodic discharges by an oxidisable substance which he supposes to exist in the lymph and blood. He supposes that apnœa is due to an excessive destruction of that substance by hyperoxygenation of the blood, while dyspnœa is due to its increase resulting from deficient oxygenation.

Although the inspiratory centre periodically discharges energy after all afferent nerves have been divided, its action even in ordinary breathing is affected in a reflex manner. The pulmonary branches of the vagi contain afferent fibres which convey from the lungs to the inspiratory centre impulses which accelerate its discharges. The division of one vagus in the neck usually produces no evident effect on the respiration, but when both vagi are divided the respiration usually—though not invariably—becomes slower and deeper. The act of

inspiration may become laboured, and may be accompanied by a whistling sound, due to obstruction to entrance of air through the paralysed glottis. The effect of the paralysed glottis may, however, be eliminated by opening the trachea previous to the division of the vagi. Notwithstanding this, respiration becomes slower and deeper when the nerves are divided. The slowness of the respiratory movements is compensated by their increased depth. Death, however, supervenes in two or three days owing to pulmonary congestion.

The above experiment shows that the vagus contains fibres which accelerate the discharges from the inspiratory centre. They do not increase the total amount of energy discharged, but merely liberate its discharge more frequently. It is not known whether these fibres of the vagus are excited by the state of the blood or the air in the lungs.

That the inspiratory centre can act without the assistance of these fibres is proved by the continuance of the respiration after the division of the vagi, and of all nerves capable of conveying impulses to the centre.

Effect of Heat on Inspiratory Centre.—Heat affects the respiratory centre as it does the cardiac ganglia. It accelerates the discharge of energy, and so quickens the respiration, producing "*heat dyspnœa.*" That has been proved, by exposing the carotid arteries of a dog, and laying them on metal

tubes through which hot water circulated; the heated blood passing to the brain produced exaggerated breathing. A similar effect is produced in the human subject by an increase in the temperature of the blood.

Effect of the Will on the Respiratory Centre.—The will can excite either the inspiratory or the expiratory centre; it can also inhibit both centres. It can inhibit the inspiratory act before it begins, but in less than a minute the tendency to excitement in the nerve cells overcomes the inhibitory action. The will can also inhibit a forced expiration, viz., a cough, unless the exciting cause be very powerful.

Effect on Respiratory Centres of Stimulation of Various Nerves.—When the vagus is divided in the neck of a rabbit below the origin of the superior laryngeal nerve, slight stimulation of its cranial end accelerates the respiration, while powerful stimulation produces spasm of the diaphragm. The vagus therefore contains fibres which are excito-motor for the diaphragm, that is, fibres which excite that part of the inspiratory centre presiding over the diaphragm. These fibres are contained in the pulmonary branches of the vagus, and their function has been already alluded to.

The pulmonary branches of the vagus also contain fibres which can excite the *expiratory centre* and produce a cough. These fibres may be thrown into action by some irritating cause in the

lung, such as accumulation of mucus in the bronchi.

The superior larnygeal nerve contains fibres that can affect both respiratory centres. Division of the nerve on both sides does not affect respiration. Stimulation of the cranial end inhibits the act of inspiration (Rosenthal), and may produce a cough. Consequently, when an irritating vapour is breathed, or a foreign body tends to enter the larynx, the act of inspiration is arrested, and expiration induced, so that the cause of irritation may be expelled. Both sets of fibres in the superior larnygeal nerve come into action only under exceptional circumstances.

Stimulation of the cranial end of the vagus, divided above the origin of the superior laryngeal nerve, produces a result similar to that obtained by stimulating the superior laryngeal nerve itself. A very powerful stimulation of the upper end of the vagus may occasion death, probably by paralysing the inspiratory centre. This result may happen even when the animal is anæsthetised.

Influence of Cutaneous Nerves.—Cold applied to the face or to the skin generally excites the inspiratory centre. The effect is very evident when a person goes into cold water in bathing. The fifth nerve—the sensory nerve of the face—appears to have a closer relation to the inspiratory centre than the other cutaneous nerves. On that account cold is applied to the face in fainting to excite respiration as well as to excite cardiac action.

Peculiar Respiratory Movements.

Coughing is an expiratory movement, the air being expelled through the mouth. It is usually a reflex action. The impulse may proceed from—

1. The respiratory mucous membrane through the pulmonary branches of vagus, or through superior larnygeal nerve.
2. The stomach, in cases of dyspepsia, through the gastric branches of the vagus.
3. The back of the tongue through the lingual branch of the superior laryngeal.
4. The outer ear, through the auricular branch of the vagus.
5. The skin, especially that of chest and throat. Coughing may be inhibited voluntarily, provided the excitement is not too powerful.

Sneezing.—In the act of sneezing, the air is expelled chiefly through the nose. The impulse usually proceeds from the nasal mucous membrane through the nasal branch of the fifth nerve. It may also proceed from the larynx and be occasioned there by a pellet of mucus, the afferent nerve in that case being the superior laryngeal. A strong light sometimes occasions a sneeze, the afferent nerve being the optic. Sneezing cannot be inhibited voluntarily, but it may often be prevented by pinching the nostrils firmly, and so pressing on the nasal nerve.

Hiccough is occasioned by a spasmodic contrac-

tion of the diaphragm occurring at intervals. It commonly results from irritation of gastric branches of vagus, or it may be due to blood-poisoning. In most cases, it may be arrested by taking a deep inspiration, and holding the breath as long as possible. When it is not arrested by that method, ice should be introduced into the stomach.

Rapidity of the Respiration.

From fifteen to twenty respirations take place in a minute in the adult. In the young child there are about twice as many respirations in the same period. In disease, the number may sink as low as seven, and may rise as high as a hundred per minute.

The respiration is slower during sleep, because of the absence of nervous excitement, and because of the slower circulation. It is accelerated by most influences that hasten the circulation—such as muscular exertion; also by cold suddenly applied to the skin, by a rise in the temperature of the blood, and by emotion.

Respiratory Changes of the Blood.

The gases of the blood are oxygen, carbon dioxide, and nitrogen. They can be extracted by a vacuum. The vacuum of an ordinary air pump is insufficient to extract all the gas, it requires to be a Torricellian vacuum, that is, a vacuum produced by the weight of mercury.

Gas Pump.—The mercurial gas pump of Ludwig, or that of Pflüger, may be used for extracting the blood-gases. Pflüger's gas pump (fig. 10) has two strong glass bulbs containing mercury (*f.e.*), which can flow from the one to the other through a strong flexible tube, and a glass tube more than 30 inches in length joined to the bulb *e*. When the bulb *f* is sufficiently elevated by the windlass *h*, the mercury flows into the bulb *e*, and with the glass taps *s*, *s'* open, and the tap *s''* closed, it drives the air from the bulb *e* and the tube above it, filling them with mercury at the same time. The taps *s*, *s'* are then closed, so that when the bulb *f* is lowered 30 inches below bulb *e* a vacuum is produced in the latter.

a is a glass receiver from which the air has to be extracted before blood is introduced by the tube *b*. *e* is a U-tube containing asbestos wetted with sulphuric acid to dry the blood gases. *d* is a mercurial manometer to indicate when a vacuum has been established in the blood receiver (*a*).

A vacuum having been produced in bulb *e*, in the above manner, the tap *s''* is opened, and some air drawn from the receiver (*a*). The tap *s''* is then closed, the bulb *f* elevated, the taps *s* and *s'* opened, and the air expelled; *s* and *s'* are then closed, *f* lowered, *s''* opened, and some more air pumped out. This process is repeated many times until the mercury in the two limbs of the manometer *d* is at the same level, indicating therefore a complete vacuum.

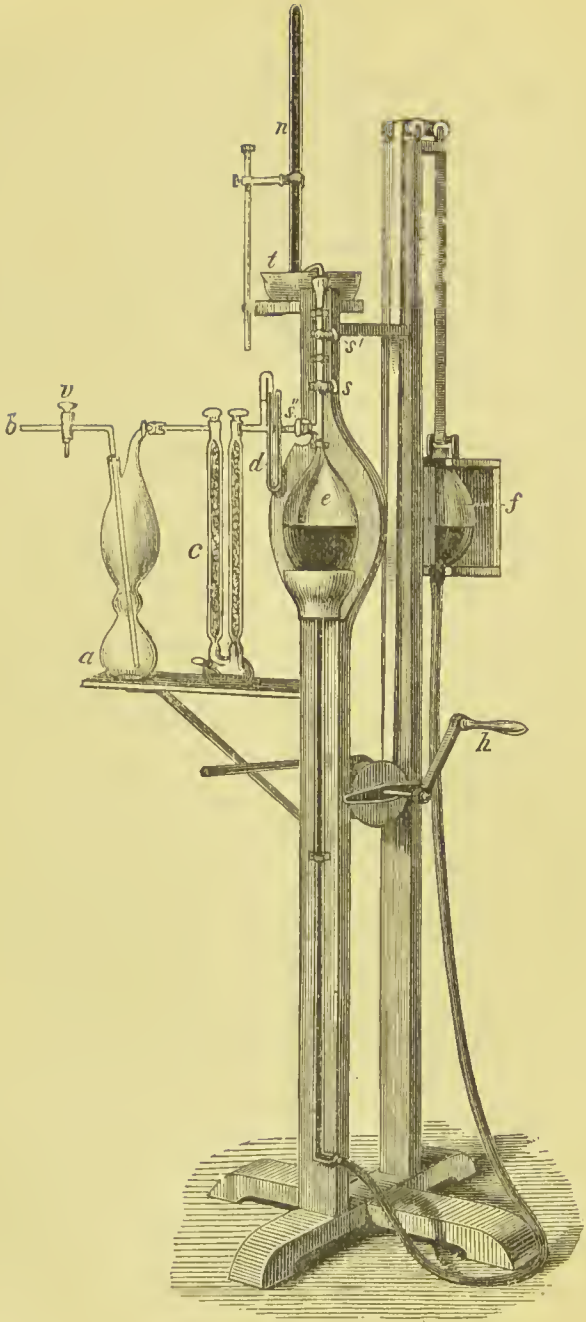


FIG. 10.—Pflüger's Gas Pump.

The blood is introduced by the tube *b* from which all air must be expelled, so that none may enter the receiver (*a*). *v* is a two-way tap, so arranged that when the entrance to the receiver is closed, the blood can flow from *b* into the tap, and out by a tube passing from its lower end, so that the tube *b* becomes completely filled with blood. The tap is then turned so as to allow a certain quantity of blood to enter the receiver. When blood is taken immediately from the artery or vein of an animal, it is allowed to flow into a graduated burette previously filled with mercury, and immediately afterwards into the tube *b*, so that when allowed to enter the receiver the amount taken for analysis may be exactly ascertained.

Most of the gas rushes out of the blood on entering the receiver. The extracted gas is then pumped out, and collected in a eudiometer (*n*) filled with mercury, and inverted over a mercurial trough (*t*). The eudiometer is then transferred to a mercurial trough of sufficient depth to allow of its being sunk until the surface of the mercury in the eudiometer is on a level with that in the trough, so that the volume of the gas may be at once read off at the ordinary barometric pressure, corrections of course being made for variations in the barometric pressure.

On introducing a small quantity of a saturated solution of recently fused potassium hydrate into the eudiometer, the CO_2 is quickly absorbed, and

its amount thus determined. A small amount of a saturated solution of pyrogallic acid is then introduced to absorb the oxygen. The small amount of gas remaining is nitrogen.

One hundred volumes of blood yield about 60 volumes of gas measured at the ordinary barometric pressure, viz., 760 millimeters of mercury, and at 0° C.

100 Vols.	O.	CO_2	N.
Arterial blood, . .	20	39	1–2
Venous blood, . .	8–12	46	1–2
	per cent. by volume.		

When measured at a pressure of 1 meter of mercury at 0° C. the method of measurement adopted in Germany, 100 volumes of blood yield about 50 volumes of gas.

100 Vols.	O.	CO_2	N.
Arterial blood, . .	16	30	1–2
Venous blood, . .	6–10	35	1–2
	per cent. by volume.		

The Oxygen.—All the respiratory oxygen of the blood leaves it in a vacuum; it must therefore be in a state of mere absorption, or in a state of *loose*

chemical union, or in both of these conditions. It is known that very little of it is merely absorbed, for if that were so, one-half of the oxygen would leave the blood when the barometric pressure is reduced one-half. But the pressure requires to be reduced to about $\frac{1}{6}$th of an atmosphere, before much oxygen begins to leave the blood. Most of the oxygen is therefore not merely absorbed but combined, and its state of combination is loose, because dissociation takes place in a vacuum.

Blood serum alone yields little oxygen, and as the amount obtained from it follows the law of pressures, the oxygen of the serum must be merely absorbed. Most of the oxygen is in the corpuscles,—combined with hæmoglobin.

The carbon dioxide is nearly all contained in the blood serum, as proved by the fact that serum alone yields nearly as much CO_2 as serum plus corpuscles. Part of the CO_2 is merely absorbed, but most of it is combined with substances in the serum. Part of the CO_2 is loosely combined, and that together with the CO_2 merely absorbed, is removed by a vacuum. But a part of the CO_2 is so firmly combined that the addition of an acid, *e.g.*, oxalic or acetic acid, is required to detach it. The firm compound is sodium carbonate. The relations of the loosely combined CO_2 are not fully known. The greater part of it is united with sodium carbonate to form the bicarbonate, while a small part appears to be united with sodium phosphate,

in the proportion of two molecules of sodium phosphate to one molecule of CO_2 (Fernet).

The free nitrogen of the blood is merely absorbed, and is insignificant.

Gaseous Changes in the Blood.—The living tissues are constantly removing oxygen from the lymph which bathes them. The tension of the O in the lymph therefore falls, and O diffuses from the blood, because of its greater tension there. When the tension of the O in the blood-plasma falls sufficiently, dissociation of O from oxyhæmoglobin takes places. On the other hand, CO_2 is constantly being produced in the tissues. Its tension is therefore highest there, and its diffusion through the lymph and the capillary walls into the blood is the necessary consequence. On entering the blood most of it is seized by sodium carbonate and sodium phosphate, by which it is carried to the lungs.

The oxygen in the air cells of the lungs, having a higher tension than that in the blood, diffuses through the alveolar membrane into the capillaries where most of it is seized by hæmoglobin, and so carried away to the systemic capillaries. The CO_2, which is merely absorbed in the blood fluid having a higher tension than the CO_2 in the air cells, leaves the blood, and dissociation of the loosely combined CO_2 then takes place. But it is not quite clear how it is that sodium bicarbonate gives off a molecule of CO_2 in the lungs, for that substance can scarcely be regarded as very unstable.

In some way not yet satisfactorily explained the entrance of O facilitates the dissociation of CO_2 in the lungs.

Relation of the Air to Respiration.

The amount of air expired may be measured by the aid of a spirometer, an instrument made on the principle of an ordinary gasometer. It consists of an inverted jar filled with water, with a tube to convey air into the interior, the volume of the air being shown on a scale with index.

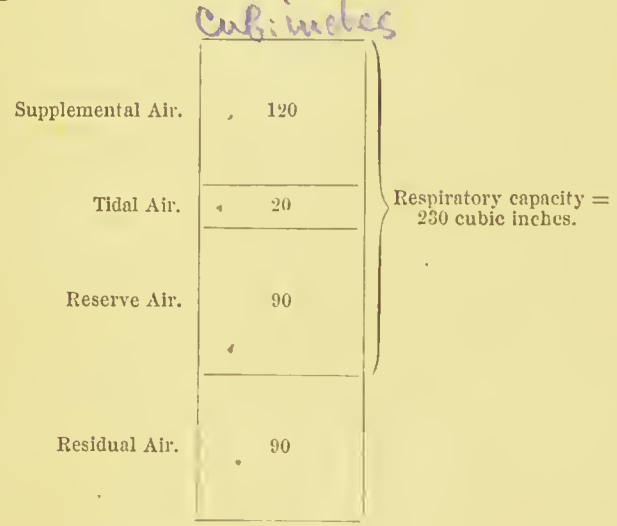


FIG. 11.—Scheme explanatory of the Respiratory Capacity.

The average amount of air moved into and out of the chest at an ordinary respiration is 20 cubic inches. That is named the *tidal* air. 120 cubic inches more can be inspired by a forced inspiration.

That quantity is termed the *supplemental* air. 90 cubic inches may be expelled by a forced expiration after the tidal air has been expired. That quantity is named the *reserve* air. There always remains in the chest after the most powerful expiration about 90 cubic inches of *residual air.*

If we take as deep an inspiration as possible, and then expel all the air we possibly can, we would drive out the supplemental, tidal, and reserve portions of air, leaving only the residual air. In an individual of average height, viz., 5 feet 8 inches, the normal amount so expired would be 230 cubic inches. That is termed the *respiratory capacity.* Hutchinson showed that the respiratory capacity has a close relation to the height of the individual. From the height of 5 feet to that of 6 feet, every inch of stature gives 8 cubic inches of respiratory capacity, thus, taking 230 cubic inches as the respiratory capacity in a person 5 feet 8 inches, it would be 238 cubic inches in a person 5 feet 9 inches in height, and so on. The respiratory capacity is also affected by the mobility of the chest wall. If the chest wall be very movable, it is possible to take a deeper breath. It is also affected by the strength of the respiratory muscles. An apparent deficiency of respiratory capacity may, therefore, in some persons be really due to deficiency of muscular power.

Since the tidal air is only 20 cubic inches, and since 180 cubic inches of air remain in the chest

alone after an ordinary expiration, it follows that the air immediately changed during ordinary respiration is the air in the nose, pharynx, trachea, and the larger bronchi. The air in the bronchioles and alveoli cannot be regarded as directly changed during ordinary respiration. Probably all that happens is that the air is merely moved to and fro between them and the larger bronchi, therefore the changes in the air of the air cells and alveolar passages are the result of diffusion between it and the purer air of the bronchi.

The Changes in the Air during Respiration.

During respiration the air loses oxygen and gains carbon dioxide, heat, moisture, and putrescible organic matter. The following table shows the difference between inspired and expired air as regards its gases:—

	N.	O.	CO_2.
Inspired air, . .	79·150	20·810	0·04
Expired air, . . .	79·587	16·033	4·38
Difference, . . .	0·437	4·777	4·34

As oxygen and carbon dioxide both have the same volumes, the amount of CO_2 added to the air being smaller (4·3 per cent.) than that of the oxygen lost (4·7 per cent.) indicates that all the oxygen absorbed by the blood does not eventually

unite with carbon. A small part of it goes to oxidise some of the hydrogen, sulphur, and phosphorus of organic compounds.

Many observations have been made regarding the influence of various conditions on the amount of oxygen absorbed, and more especially on the amount of carbon dioxide excreted. The apparatus employed by Scharling for estimating the amount of CO_2 and water excreted in a given period, consists of a chamber large enough to hold a man. A stream of air is drawn through the chamber by an aspirator in the form of a vat filled with water. The outflow of the water draws air out of the chamber through a tube passing to the top of the vat. The air was drawn into the chamber through bulbs containing potassium hydrate to remove CO_2, and then through tubes containing fragments of pumice wetted with sulphuric acid to dry the air. The air drawn out of the respiration chamber was in like manner drawn through sulphuric acid tubes to remove the water, and through potash bulbs to remove the CO_2 that had been exhaled from the lungs. The difference in weight between the sulphuric acid tubes and potash bulbs, before and after the expired air had been drawn through them for a definite period, gave the amounts of H_2O and CO_2 excreted.

The respiration apparatus invented by Pettenkofer and Voit is a large respiration chamber through which the air is drawn by a suction pump

driven by an engine. The total amount of air drawn into the chamber in a given time was measured, and the CO_2 was estimated in only a fraction of the air containing the results of expiration; the necessary calculation being made for the total amount of CO_2.

The average amount of oxygen absorbed in twenty-four hours is about 26 oz. The average amount of carbon excreted by the lungs, oxidised as CO_2, in twenty-four hours, is about 8 oz. Many circumstances determine variations in the mount excreted, but these will be considered with the subject of excretion.

Addition of Heat to the Air.—Air which is inspired and expired through the nose is heated to within about 4° F. of the temperature of the blood. The importance of heating the air before entering the lungs is shown by the irritation which follows the introduction of cold air directly into the trachea in a case of tracheotomy. Most of the heat added to the air is derived from the blood-vessels in the lower part of the nose, especially those over the inferior turbinated bone, also from the vessels of pharynx, trachea, and bronchi. The heat is principally derived from the air passages; a part, however, also comes from the blood of the alveolar capillaries, *i.e.*, from the blood passing from the pulmonary artery to the pulmonary vein. The blood of the latter is from some hundreds to some tenths of a degree centigrade colder than the blood of the pulmonary artery (Bernard).

Addition of Moisture to the Air.—About 9 oz. of water are excreted by the lungs daily. The amount varies with the moisture of the external air.

Addition of Putrescible Organic Matter.—When air is expired through water for a considerable time, the water acquires an unpleasant odour, due to the putrescible organic matter in the expired air. The presence of the organic matter may be shown by driving expired air for a considerable time through a dilute solution of potassium permanganate ($KMnO_4$). The $KMnO_4$ is reduced to manganese dioxide, and the pink colour of the permanganate solution becomes changed to a dirty brown. The organic matter is probably mainly derived from the mucous membrane of the respiratory passages.

The Effect of Breathing Air Vitiated by Respiration.—A sense of mental and muscular fatigue soon supervenes in most persons when they breathe respired air containing 0·1 per. cent of CO_2 (The normal amount in inspired air is 0·04 per cent.) The evil effects are due to the organic matter as well as to the CO_2, for if 0·1 per cent. of CO_2 is added to air without the organic matter of the breath, it can be inhaled without deleterious effect for a longer time than air containing 0·1 per cent. CO_2 + the organic matter of the breath.

The amount of the CO_2 and of the organic matter in expired air being in almost constant ratio, the amount of the CO_2 serves as an index of

its purity. When air that has been breathed has an unpleasant odour, its effects are always injurious; the odour is somewhat unpleasant when the CO_2 rises to 0·07 per cent., and decidedly disagreeable when it rises to 0·1 per cent., the odour of course being due not to the CO_2 but to the organic matter.

Breathing Space required.—It is necessary to keep the CO_2 of the air in an apartment below 0·06 per cent. If a man be placed in a closed chamber containing 1000 cubic feet of pure ordinary air, it is found that at the end of one hour the CO_2 in the air has risen to 0·06 per cent. To keep the air of such a chamber near to the normal standard, it requires to be changed three times in the course of an hour. There is difficulty in maintaining such rapid ventilation in cold climates, but the difficulty may be overcome by heating the incoming air, and may be diminished by giving a larger breathing space. A thousand cubic feet is, however, the smallest breathing space which should be allowed to an adult in any building.

Asphyxia or *Suffocation* is the most serious result of diminished or arrested respiration. It may be occasioned (1) by breathing a vitiated atmosphere; (2) by obstruction to the entrance of air into the blood, as in drowning or in pneumonia, where the air vesicles are blocked by inflammatory exudation; (3) by alteration of the blood pigment, as in carbonic oxide poisoning.

The symptoms of asphyxia in order of their appearance are—

1. Hyperpnœa soon followed by dyspnœa.
2. A short stage—during which the desire for air disappears, the individual however still remaining conscious.
3. Unconsciousness, convulsions, paralysis of respiratory centre.
4. Paralysis of the heart and death.

When the blood-vessels and heart are examined after death by suffocation in man or in animals, it is found that the right side of the heart, the pulmonary artery, and systemic veins near the chest are engorged with blood. It was formerly thought that this condition results from an arrest in the flow of the blood through the lungs due to spasm of the pulmonary arterioles. That explanation, however, is not the true one. The changes in the circulation during asphyxia are complicated, and require to be studied in their order. If the chest of a dog be opened, the ribs removed, artificial respiration maintained, a manometer placed in a small branch of the pulmonary artery, and another manometer in a systemic artery, *e.g.*, the femoral, and the blood pressure registered in both cases, it is found that when the breathing is stopped the vasomotor centre in the medulla becomes excited by the venous condition of the blood, and, by causing constriction of systemic vessels, occasions a great rise in the systemic arterial pressure. The pulmonary vessels are

scarcely at all affected. The pressure in the pulmonary artery undergoes only a very slight increase compared with that in the aortic system, showing, as Lichtheim correctly pointed out, that the pulmonary artery differs from the systemic arteries in having only a very slight relation to the vasomotor centre in the medulla.

The heart is enfeebled by venous blood circulating in the coronary vessels; the left ventricle becomes unable to contract against the excessive resistance due to the high pressure in the aorta, and at that stage it may be seen that the left ventricle is engorged and motionless, while the right side of the heart goes on beating.

The vasomotor centre in the medulla then becomes paralysed owing to want of oxygen. The systemic arteries therefore dilate, the blood flows out rapidly through the systemic capillaries into the veins, the aortic pressure falls, and the left ventricle relieved from its engorgement begins to beat again but very feebly, because its walls are being supplied by venous blood.

The blood now accumulates in the right side of the heart, for the weakened right ventricle is unable to drive it through the pulmonary artery, and the recoil of the systemic arteries is driving it on into the systemic veins and right side of heart.

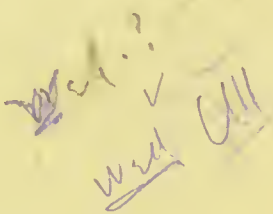
When the chest is unopened, violent attempts at inspiration powerfully draw blood through the systemic veins into the right side of the heart, and so contribute to its engorged condition.

Recovery from the state of asphyxia seldom occurs if the person has been deprived of air for more than five minutes. Rare cases of drowning are recorded, in which recovery took place after from ten to fifteen minutes' deprivation of air. The methods suitable for promoting recovery are the following:—

1. *Artificial Respiration* by Sylvester's method. The mouth is opened, the tongue pulled out and kept forwards with the aid of an elastic band over the tongue and chin, or by some other means. Both elbows are then seized and the arms forcibly pulled upwards to the head to expand the chest and so produce inspiration. They are then carried back to the chest and pressed upon it, in order to expel air, thus imitating the act of expiration. These movements are repeated from 25 to 30 times in the minute. The artificial respiration should be kept up for at least forty minutes before the case is considered hopeless.

2. *Means for inducing Circulation.*—A sponge wrung out of very hot water should be repeatedly applied over the region of the heart to stimulate it. Hot bottles should be applied to the feet and limbs, and the latter should be rubbed vigorously in order to assist the circulation. Reid proposed that the external jugular vein on the right side of the neck should be opened, and a probe introduced to open the valve at its root, to allow blood to flow from the engorged heart; but this measure is rarely adopted.

The inner respiration or tissue respiration is most active in *muscle, nerve cells,* and *glands.* Its rapidity varies (1) with rapidity with which energy is produced, *e.g.*, in a muscle,—when it evolves energy, the respiration is more rapid. (2) With the temperature of the tissue; within limits, an increase of temperature increases the respiration. (3) With the age of the tissue. It becomes less rapid in old age.



ALIMENTATION.

Alimentation signifies the introduction of food materials into the blood through the alimentary canal. The chief constituents of the food may be divided into four groups:—1. Proteids; 2. Amyloids, viz., starch and sugar; 3. Fats; 4. Minerals.

Insalivation.

The buccal saliva is a mixture of secretions from the salivary glands proper, and from the glands of the mouth. The saliva is colourless, viscous, watery; specific gravity, 1006; contains squamous epithelium shed from the mouth, and salivary corpuscles derived from submaxillary and sublingual glands.

Buccal Saliva (*Human*).

Water, 995·16.	Epithelium, ...	1·62	
	Salivary corps, . . .		
Solids, 4·84.	Ptyalin, ...	1·38	
	Mucin, ...		
	Albumin, ...		
	Globulin, ...		
	Inorganic solids, . . .	1·84	
Gas, ...	CO_2.		

The inorganic solids are—1. *Earthy salts*, viz., calcium carbonate and phosphate, magnesium

phosphate. The "tartar" around the teeth results from precipitation of earthy salts.

2. *Alkaline salts*, viz., sodium chloride, and potassium chloride. A trace of sulphocyanide of potassium is found in the parotid saliva.

The normal reaction of the saliva is slightly alkaline, but it may become acid in dyspepsia.

Functions of Saliva.—1. It assists articulation by moistening the mouth.

2. It assists mastication and deglutition by moistening the food. Its viscosity—which is due to mucin—lessens friction in swallowing.

3. It assists gustation by dissolving substances, and thus allowing their molecules to reach the end-organs of the nerves of taste.

4. It transforms starch into a form of sugar named maltose. It has no action on proteids, and scarcely any upon fats.

Action on Starch.—A starch corpuscle chiefly consists of granulose enclosed in envelopes of cellulose. Saliva has no action on the cellulose, but it changes the granulose into dextrin and sugar, rapidly, if the cellulose envelopes have been softened and swollen by boiling, but very slowly, if the starch is unboiled. The sugar produced is maltose $C_6H_{12}O_6$, with a small quantity of glucose. These two sugars are isomeric; both reduce cupric oxide to cuprous oxide, and both rotate a polarised ray to the right. Maltose is a less powerful reducing agent than glucose in the

proportion of 10 to 6; but its rotatory power is nearly thrice as great as that of glucose.

Between the starch and the maltose, there are several intermediate substances still requiring investigation. But the main transformation is probably this: the starch molecule commonly expressed by the formula $C_6H_{10}O_5$, is more probably $C_{18}H_{30}O_{15}$. It links on a molecule of water, and splits into two molecules of dextrin, and one molecule of maltose. Thus—

$$\underset{\text{Starch.}}{C_{18}H_{30}O_{15}} + H_2O = 2(\underset{\text{Dextrin.}}{C_6H_{10}O_5}) + \underset{\text{Maltose.}}{C_6H_{12}O_6}.$$

The molecules of dextrin then severally take up a molecule of water, and so become sugar.

The fermentative power of the saliva upon starch is due to ptyaline, a non-living ferment of unknown chemical nature. It acts best in a slightly alkaline fluid, at the temperature of the body. It is destroyed by boiling. It is in very small amount in the saliva. A small quantity of it can transform a large quantity of starch. It is doubtful whether or not it disappears during the process of fermentation.

The Salivary Glands.

The parotid, submaxillary, and sublingual glands are the salivary glands proper. All are compound tubular glands. Each gland has a framework of ordinary fibrous tissue, arranged as a loose capsule, sending inwards septa that

divide the gland into lobes, and subdivide these into lobules.

Ducts.—The *parotid gland* has a single duct—*Stenson's duct*—that opens inside the cheek, opposite the second molar of upper jaw. The *submaxillary gland* has one duct—*Wharton's duct*—opening beneath the tongue near to the frœnum. The *sublingual gland* has several ducts,—8 to 20. The largest, named the *duct of Bartholine*, opens into the mouth separately near to Wharton's duct. The others, named the *ducts of Rivini*, open—some into Wharton's duct, the others near it.

The main duct, *e.g.*, of the parotid, gives a branch to each lobe. The *lobar ducts* subdivide into branches for the several lobules. Each *lobular duct* divides into several *intralobular ducts*. Each intralobular duct becomes narrowed into the *intermediate duct* before it joins the secreting tubules of the gland proper.

Structure of the Ducts.—There is an endothelial basement membrane in all the ducts, lined by a layer of cubical or squamous epithelium in the intermediate ducts, and by a layer of columnar epithelium elsewhere. The columnar epithelium presents the ordinary appearance in the lobar and lobular ducts, but in the intralobular ducts each cell is striated in its outer part, owing to a radial arrangement of the cell network. Outside the basement membrane in the larger ducts there is a circular layer of non-striped muscle, covered by a fibrous sheath continued from the capsule.

Structure of the Secreting Tubules.—The true gland consists of branching tubules with lateral diverticula. There is a basement membrane of branching endothelial cells, lined by a secreting epithelium, that differs in the different glands.

The parotid is a serous or *true salivary gland.* Its secreting element consists of a single layer of somewhat columnar cells with a close protoplasmic network. During a *resting condition* of the gland, the cells become enlarged and very granular. During *secretion,* the granules are moved towards the lumen of the tubule, and leave the cells somewhat shrunken (Langley).

The sublingual gland of man is a *true mucous gland.* The cells in the secreting tubules are of two sorts—(1) *clear mucin-forming cells* of columnar shape, each with a nucleus deeply placed near the basement membrane. (2) *Granular or parietal cells of polygonal shape* and small size, arranged between the basement membrane and mucin-forming cells in groups of crescentic form—named *the crescents of Gianuzzi.* During a *resting state* the mucin-forming cells become filled with mucin, or a preliminary substance—mucigen—which is discharged when secretion takes place, leaving the cells smaller and somewhat granular in appearance, owing to a shrunken condition of the cell network (Klein).

The human submaxillary gland is a *muco-salivary gland.* Some of its tubules are *true salivary tubules*

like those of the parotid; others are *true mucous tubules* like those of the sublingual.

Characters of the different Secretions.—The secretions from the several glands may be isolated and collected by cannulæ introduced into the openings of the different ducts.

The parotid saliva is the most watery; it contains albumin, but no mucin, no salivary corpuscles, and it digests starch.

The submaxillary saliva contains mucin and salivary corpuscles, and it digests starch.

The sublingual saliva contains much mucin and many salivary corpuscles. Its action upon starch is doubtful.

As regards the origin of the salivary corpuscles Klein supposes that they are emigrated lymph corpuscles, altered by the water of the saliva.

Vessels, Lymphatics and Nerves of Salivary Glands.—All the glands are very vascular, and have many lymphatics and nerves. There are ganglia on the nerves in the submaxillary and sublingual, but not in the parotid gland (Klein). According to Pflüger the nerve fibres are directly continuous with the gland cells. Their relation must be very close, because impulses have to pass from the nerve fibres to the cells, but Pflüger's conclusion as to their continuity has not been confirmed as yet.

Secretion of Saliva.—From one to two pounds of saliva are secreted daily. In the condition of so-called rest, the gland cells slowly produce ptyaline and mucin, or substances preliminary to

these, which are transformed into them when secretion actually takes place. The cells are usually excited to secrete by nervous influence. The nerves for the several glands belong to the cerebro-spinal and to the sympathetic systems.

The Secretory Nerves for the Submaxillary and Sublingual Glands.—(1) *The chorda tympani* branch of the portio dura division of the seventh nerve (fig. 12, *C.T.*) joins the lingual branch of the fifth (*Gu.*). Part of it passes in that nerve to the tongue, the remainder leaves it at the submaxillary ganglion (*S.G.*), and passes to the above-named glands. The nerve filament containing the chorda fibres passes along Wharton's duct, and may be exposed without difficulty. When that nerve is divided, and its peripheral end stimulated, the effect is the same as when the chorda tympani itself is excited.

When a cannula is placed in Wharton's duct, *e.g.*, in a dog, and the nerve passing from the submaxillary ganglion to the submaxillary gland divided, no secretion flows from the duct; but on stimulating the peripheral end of the nerve with electricity, a copious *secretion of watery saliva* ensues. The saliva so secreted is for convenience named *chorda* saliva. The stimulation of the nerve produces at the same time a dilatation of the blood-vessels of the gland, which is often so great that a pulse appears in the veins of the gland, and the blood-stream through the dilated

vessels is so rapid that the blood in the veins becomes scarlet. The sublingual gland is similarly affected. These facts were discovered by Bernard.

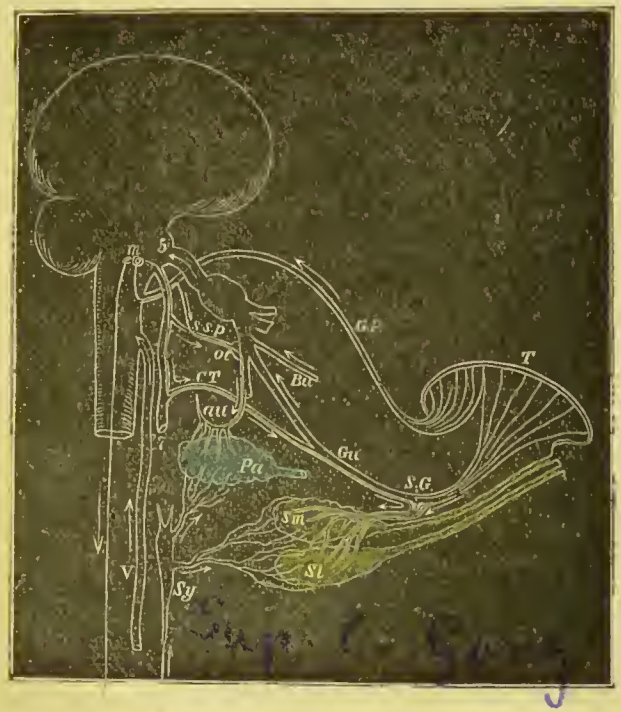


FIG. 12.—Scheme of the innervation of the salivary glands. *T*, tongue; *G.P.*, glossopharyngeal nerve; *Gu*, gustatory; *Bu*, buccal; *au*, auriculo temporal branch of fifth nerve; *S.G.*, submaxillary ganglion; *ot*, otic ganglion; *C.T.*, chorda tympani; *s.s.p.*, small superficial petrosal branch of seventh nerve; *V*, vagus; *Sy*, cervical sympathetic; *Pa*, *Sm*, *Sl*, parotid, submaxillary, and sublingual glands; *m*, salivary centre in medulla.

The vascular dilatation and secretion, although concomitant, are independent. That is proved by

the fact, that when atropia is given, the secretory fibres, but not the vaso-inhibitory fibres, are paralysed. Therefore stimulation of the peripheral end of the atropinised nerve produces vascular dilatation as before, but no secretion (Heidenhain). The secretory fibres of the chorda tympani come through the portio dura nerve from a salivary centre placed in the upper part of the medulla (*m*).

2. *The sympathetic* gives branches to all the salivary glands. The filaments pass from the superior cervical ganglion (fig. 12, *Sy*) along the blood-vessels, directly to the glands. Stimulation of the sympathetic nerve after it has been divided in the neck causes contraction of vessels in all the glands, and a secretion of a small quantity of saliva, which in the case of the submaxillary and sublingual glands is extremely viscous. Atropin does not paralyse the secretory fibres belonging to the sympathetic. The sympathetic secretory fibres probably spring from a centre in the upper part of the medulla. They pass down the spinal cord, leave it at lower part of neck, enter the cervical sympathetic, and ascend in that nerve to its superior ganglion from which they pass to the glands.

The chemical difference between the *chorda* and the *sympathetic* saliva appears to be merely a difference in the amount of water. The cause of the difference is not to be found in the *increased blood-stream* resulting from stimulation of chorda and the *diminished blood-stream* due to stimulation

of the sympathetic. The watery character of the chorda saliva does not depend on the vascular dilatation. Ludwig proved that by the following striking experiment. If a manometer be placed in connection with Wharton's duct, another manometer in connection with a branch of the carotid artery of the same side, or more conveniently in the carotid of the other side, and if the divided chorda or the nerve containing its fibres be then stimulated, the pressure of the saliva gradually rises to—it may be—the *double of the arterial* pressure. The fibrous coat of the duct may indeed be eventually ruptured by the pressure of the secretion.

The movement of water from the blood-vessels and lymph into the gland tubes is not determined by the blood pressure—it is therefore not a case of filtration as the secretion of water by the kidney is. The only probable theory is, that the water is moved from the surrounding lymph, through the gland cells into the ducts, by *a vital activity of the cells.*

Heidenhain has suggested that both the chorda and the sympathetic contain a set of *water-secreting* and a set of trophic or *solid-secreting* fibres, in addition to those fibres that affect blood-vessels. The fibres that stimulate the cells to secrete water are in the dog and in the human subject most numerous in the chorda. The trophic or solid-secreting fibres hasten the processes in the cells which lead to production of

mucin and ptyaline, and they are in the sympathetic relatively more numerous than the water-secreting fibres.

A change takes place in the secretion when the chorda has been stimulated for a considerable time; the organic solids diminish apparently because the trophic changes in the cells are not able to keep pace with the secretion of water (Heidenhain).

Heat is evolved in the excited gland. The saliva flowing from the duct may be 1½° F. hotter than the blood. The heat springs from the metabolism in the excited gland cells.

The secretory nerves for the parotid are, as in the other glands, derived from the cervical sympathetic, and from a cerebro-spinal nerve. The small superficial petrosal branch (fig. 12, *s.s.p.*) of the portio dura nerve contains the cerebro-spinal secretory fibres. They pass through the otic ganglion (*ot*) on the inferior maxillary division of the fifth, and thence by the auriculo-temporal nerve (*au*) to the parotid gland. It was formerly thought that the secretory fibres of the small superficial petrosal nerve spring from the portio dura nerve, but in the dog at all events, they are derived from the glossopharyngeal nerve through its tympanic branch, which sends filaments to join the small superficial petrosal nerve. When the tympanic branch of the glossopharyngeal nerve is cut across and its peripheral end stimulated by applying a drop of glycerine to it, or when the glossopharyn-

geal nerve is exposed within the skull, then divided, and its preipheral end stimulated in the same manner, the parotid gland secretes a watery saliva. The sympathetic parotid saliva is thick, but not viscous, for there is no mucin.

Exciting Causes of Salivary Secretion.—The salivary secretion may be induced—

1. *By reflex action.* It is usually so induced. The afferent nerves are—

(*a*) The glossopharyngeal nerve, when stimulated, reflexly excites all the salivary glands to secrete.

(*b*) The gustatory and buccal branches of the fifth nerve, when stimulated, reflexly excite the submaxillary and sublingual glands, *but not the parotid.*

The peripheral ends of the above nerves are normally excited from the mucous membrane of the mouth. The application of sodium chloride, acetic and other acids, and ether vapour to the tongue, and also the chewing of pyrethrum reflexly induce a copious secretion.

(*c*) The gastric branches of the vagus (fig. 12, V) may also act as afferent nerves. When an emetic is given a copious flow of saliva occurs when vomiting is just about to take place. The vomiting in such a case is due to stimulation of a centre in the medulla through the gastric branches of the vagus; the stimulation of the salivary centre in the medulla is no doubt due to excite-

ment transmitted from the stomach through the same channels.

The salivary centre is placed in the upper part of the medulla. When the brain is sliced away above the medulla, secretion of saliva can still be reflexly induced. But it is rendered impossible by slicing away the upper part of the medulla. The submaxillary and otic ganglia do not appear to be reflex centres for secretion. Their function is unknown.

2. *Emotional states affect the salivary centre.* The emotion may excite a flow of watery or of viscous saliva, or if it be the emotion of fear, it may arrest the secretion even when it ought to be excited by the presence of food in the mouth. Probably in that case the emotion inhibits the salivary centre.

3. *Movement of the jaws occasions a flow of saliva* It is difficult to say whether the secretion is in that case due to a reflex impression passing to the medulla, through the fifth nerve distributed to the muscles of mastication, or to the mechancial effect of the movement of the jaw upon the glands in the neighbourhood.

4. *The salivary glands are affected by various drugs.* They are stimulated by pilocarpin, mercury, and some other substances when introduced into the blood. Atropia paralyses the secretory fibres belonging to the seventh and eighth nerves, and it can arrest the secretion excited by pilocarpin.

Paralytic Secretion.—When all the nerves going to the salivary glands have been divided, the

glands begin some time afterwards to secrete a thin saliva, and continue to do so until they are exhausted. A similar secretion takes place in the pancreas and intestinal glands when all their nerves have been divided. It is termed *paralytic secretion*. The cause of it is unknown.

Glands of the Mouth.

1. *The mucous glands of the mouth* are the *lingual* glands at the root, sides, and under the tip of tongue (fig. 13, *m*). The *labial glands* inside the lips, the *buccal glands* inside the cheek, and *palatine glands* in the soft and hard palate. These glands are largest in the lower lip and in the soft palate, and they are all compound tubular glands. The ducts are composed of basement membrane lined with ordinary columnar epithelium. That epithelium is found lining all the ducts. Near the opening the epithelium is squamous like that in the mouth generally, and where the ducts open into the gland proper it becomes cubical or squamous. The gland proper consists of branching tubules with lateral diverticula. The secreting cells are clear columnar mucin-forming cells similar to those of the sublingual gland. Crescents of Gianuzzi are also present though small. There is a basement membrane of endothelial cells. Probably all glands of the mouth are under the influence of nerves, certainly those of the tongue are so. The nerve that presides over at least

some of the glands of the tongue is the chorda tympani. When that nerve is stimulated, the glands on the border of the tongue on the same side secrete.

2. *Serous glands* are found at the root of the tongue (*s*). They are compound tubular glands. and they open into the valleys of the circumvallate

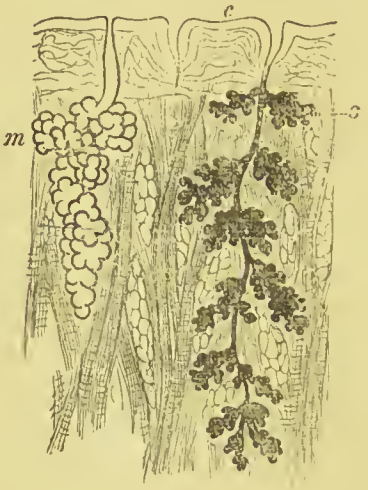


FIG. 13.—Vertical section of root of dog's tongue. *m*, mucous gland ; *s*, serous gland (or Ebner's gland); *c*, circumvallate papilla.

papillæ (*c*). Their structure is similar to that of the parotid gland. The secretion from the serous glands has no mucin : but it contains albumin, hence the name *serous*. The function of the secretion of these glands will be alluded to when the sense of taste is described.

Mastication.

In the movements of mastication the *jaws are closed* by the masseter, temporal, and internal pterygoid muscles.

The jaws are opened by the *mylo-hyoid, genio-hyoid, and diagastric*, and in order that these muscles may act, the hyoid bone must be drawn down and fixed by the *sterno-hyoid, thyro-hyoid, omo-hyoid*, and *sterno-thyroid* muscles.

A lateral and forward motion is given to the lower jaw by the *external pterygoid* muscle, and a forward motion simply when the external pterygoid muscles contract on both sides.

The lower jaw is drawn back by the lower fibres of the *temporal* muscle.

The food is prevented from passing outside the teeth by the *buccinator*, and by the *orbicularis oris* muscles.

Action of the Tongue in Mastication.—The tongue moves the food about, squeezes it against the hard palate, and presses it into a pulp.

The Mucous Membrane.—The *glands* of the tongue already mentioned are mucous and serous glands. There are also solitary glands found in the submucous tissue at the base of the tongue. These are lymph follicles, and consist of adenoid tissue with many capillaries, and in the meshwork of the adenoid tissue, lymph corpuscles are produced.

Nerves of the Mucous Membrane of the Tongue.—

Four cranial nerves are distributed to the mucous membrane. The *lingual branch of the fifth* goes to the anterior two-thirds of the tongue, and is the nerve of tactile sensibility to that region. The *nerve of taste* for the anterior two-thirds is the *chorda tympani*, which passes to the tongue in the gustatory nerve. It is also the secretory nerve for the anterior part of the tongue. *The glossopharyngeal nerve* is distributed to the posterior third of the tongue, and is a nerve of tactile sensibility and also of special sense. *The lingual filament of the superior laryngeal* nerve is distributed to the root of the tongue, close to the epiglottis, and is a nerve of tactile sensibility.

Structure of the Tongue.—In the centre there is a longitudinal fibrous septum, and there are many muscular fibres extrinsic and intrinsic.

Intrinsic Muscles.—There are four sets. (1) *Transverse fibres* springing from the fibrous septum, and passing outwards to the submucous tissue at the side of the tongue. When they contract they thicken and also elongate the tongue. (2) *Vertical fibres.*—They are not quite vertical. They are arranged in curves passing downwards and outwards from the dorsum of the tongue. They flatten the tongue. (3) *Superficial lingual muscle,* composed of longitudinal fibres, which run along the dorsum of the tongue. It shortens the tongue and turns its tip upwards. (4) *Deep lingual muscle,* composed of a large bundle of muscular fibres on each side. It is placed between the genio-hyo-

glossus and the hyoglossus. When it contracts the tongue is shortened and the tip turned downwards.

Extrinsic Muscles.—The *stylo-glossus* passing from the styloid process down to the side of the tongue on the inferior aspect. It is near to and just covered by, the mucous membrane. When both styloglossi muscles contract the tongue is drawn backwards and its sides raised. The *hyoglossus* passes upwards from the hyoid bone through the interior of the tongue to the dorsum. When both muscles contract the tongue is drawn downwards. The *genio-hyoglossus* springs from the lower jaw, and passes to the dorsum in the interior of the tongue on each side of the fibrous septum and close to it. When its middle fibres contract the tongue is drawn down. The anterior fibres draw the tip down and back, and the posterior fibres draw the root forwards. *The palato-glossus* is found in the anterior pillar of the fauces. It passes down the soft part to the side of the root of the tongue.

The *motor nerve* of the tongue is the hypoglossal.

Deglutition.

In the act of deglutition the food is moved from the mouth, through the fauces, pharynx, and œsophagus, into the stomach. The *pillars of the fauces* are two vertical folds of mucous membranes, each containing a muscle. The anterior pillar

contains the palato-glossus, the posterior pillar the palato-pharyngeus muscle. The tonsil is placed between the two pillars on each side, and consists of mucous and solitary glands with many blood-vessels. The pharyngeal mucous membrane has many mucous glands, and there is a semi-circular belt of solitary glands on a level with the tonsils. The epithelium is ciliated in the upper half of the pharynx, stratified squamous in the mouth, fauces, lower half of pharynx, and œsophagus,—all these parts being exposed to much friction. The submucous tissue of the pharynx forms a distinct membrane in its upper part, where it is attached to the base of the skull.

The act of deglutition consists of a voluntary and an involuntary stage.

Voluntary Stage.—1. The food is collected into a bolus by the action of the tongue against the hard palate.

2. The jaws are closed in order that the muscles proceeding from the lower jaw to the hyoid bone and larynx may have their fixed point above, so that the larynx may be drawn up.

3. The bolus of food is moved back by a peristaltic action of the tongue; it being pressed against the hard palate from before backwards, and so driving the food to the fauces and pharynx.

Involuntary Stage.—The involuntary stage of deglutition begins when the food reaches the posterior third of the tongue, the region of the glossopharyngeal nerve.

The Food is Prevented from Passing into the Larynx.—(1) Elevation of larynx by contraction of supra-hyoid muscles, thyro-hyoid, and stylo-pharyngei muscles. (2) By descent of epiglottis; it is pushed down by the receding tongue, and pulled down by the arytæno-epiglottidei muscles. (3) The glottis is closed by its muscles, so that any food which may chance to get beneath the epiglottis rarely gets through the glottis.

The Food is Prevented from Passing up into the Nose.—The soft palate is elevated by the levator palati, and rendered tense by the tensor palati muscles. The superior constrictor narrows the upper part of the pharynx, and so brings it against the tense soft palate.

Passage of Food through Pharynx and Œsophagus.—When the food is moved into the pharynx by the peristalsis of the tongue, it is prevented from returning to the mouth by the tongue being still kept hardened against the palate, and by constriction of the fauces by the palato-glossi muscles. The palato-pharyngei muscles pull the lower part of the pharynx up over the bolus of food, which is at the same moment driven down by the pharyngeal constrictors. The muscular fibres then contract peristaltically, and drive the food into the stomach.

The œsophagus has three coats—mucous, submucous, muscular.

The mucous coat consists of a dense areolar tissue, raised into papillæ beneath the lining of

stratified squamous epithelium, in which they are completely embedded. There are some longitudinal bundles of unstriped muscle in the outer part of the mucous membrane, named the *muscularis mucosæ.*

Submucous coat of loose areolar tissue with mucous glands. Their ducts open on mucous surface.

Muscular Coat.—Two layers: inner—circular; outer—longitudinal. Fibres striped in upper half of gullet, where rapid movement of the food past larynx is necessary; non-striped in lower half.

A nerve plexus with ganglia is found between the two layers of the muscular coat, and also in the submucous coat.

Nerves concerned in Deglutition—Voluntary Stage. The fifth nerve is motor to muscles that close jaw; ninth nerve motor to muscles of tongue.

Involuntary Stage—Motor Nerves.—The fifth and ninth nerves to some of the muscles of the voluntary stage still act. Pharyngeal branch of vagus to constrictors of pharynx and stylo-pharyngeus. Œsophageal branches of vagus to gullet. Fifth nerve to tensor palati; seventh nerve (portio dura) to levator palati.

Nerve centre for deglutition is placed in medulla a little above respiratory centre. Its position has been ascertained by slicing away brain from above downwards. Deglutition continues although brain above medulla is sliced away. By slicing away medulla downwards, deglutition is suspended,

while respiration still continues provided lower part of medulla remains.

Excito-motor Nerves for Deglutition.—Glosso-pharyngeal for posterior third of tongue and pharynx. Lingual filament of superior laryngeal to root of tongue. Branches of fifth nerve to palate. Œsophageal branches of vagus to mucous membrane of gullet.

To excite deglutition in an unconscious person, the substance to be swallowed must be placed on posterior third of tongue in order to excite glosso-pharyngeal nerve, because the fibres of the fifth nerve distributes to mucous membrane of anterior two-thirds of tongue are not excito-motor nerves for deglutition.

Gastric Digestion.

Structure of Stomach.

The stomach has four coats:—

1. *Serous coat* derived from peritoneum.

2. *Muscular coat* (fig. 14, *C*) Three layers of non-striped fibres.

(*a*) *Outer layer* of longitudinal fibres continuous with those of gullet, found only on great and small curvatures.

(*b*) *Middle layer* of circular fibres, a continuous layer.

(*c*) *Inner layer* of oblique fibres continuous with circular fibres of gullet; an incomplete

layer. The pyloric sphincter is a thickening of the middle (circular) layer.

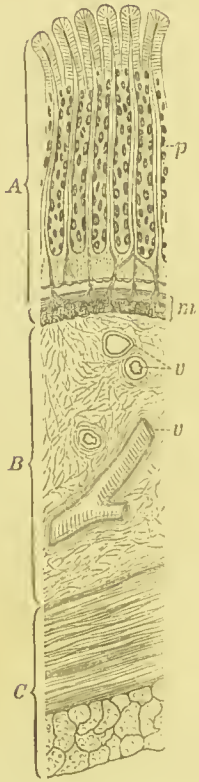


FIG. 14.—Vertical section of stomach of cat. *A*, mucous coat; *B*, submucous coat; *C*, muscular coat; *p*, peptic glands; *m*, muscularis mucosæ; *v*, *v*, blood-vessels (low power).

3. *Submucous coat* (*B*).—Areolar tissue with somewhat large vessels.

4. *Mucous coat* thrown into folds (*rugæ*) in empty state of stomach.

The mucous membrane (*A*) is lined by a simple layer of columnar epithelium, which is continued into the ducts of all the glands. The cells lining the ducts, ~~and many of those on the general surface,~~ are mucin-forming cells. The endothelial basement membrane of Débove is beneath the columnar cells, and encloses the cells in all the glands.

The *glands of the stomach* are of two sorts, *peptic* and *pyloric*.

The peptic glands (*p*) are found everywhere except near the pylorus. They are tubular, some are simple, most are compound. At the cardiac end of the stomach

they are generally compound. From two to five tubules may open into one duct, which is about a fifth of the whole length of the gland. The duct is lined by mucin-forming cells. The special part of the follicle contains cells of two sorts, named the *adelomorphous* or *chief* cells, and the *delomorphous* or *parietal* cells. The adelomorphous cells have faint outlines, and are not easily distinguished, hence their name (*αδηλος*, hidden). They are columnar or polygonal in shape, and granular in appearance. They are arranged in an almost continuous layer from the closed end of the tubule to the mucin-forming cells in the duct. They secrete *pepsin*. The *delomorphous* cells are found outside the former, at intervals in the course of the tubule. They are mostly somewhat angular in shape, and are attached to the basement membrane by processes sometimes pointed. Their outlines are always more evident than those of the adelomorphous cells. They stain more deeply with carmine, eosine, and various other dyes. They appear to secrete hydrochloric acid.

The pylorie glands are found near the pylorus. They have long ducts lined by mucin-forming cells; hence the old idea that they are simply mucous glands. The follicle is divided near its closed end into two or three crypts lined by cells resembling the adelomorphous cells of the peptic glands, and which, according to Heidenhain, secrete pepsin.

The muscularis mucosæ consists of two or three

layers of non-striped muscle in the outer part of the mucous coat (*m*), that send inwards branching bundles of fibres running parallel with the glands, and turning round at their necks to form a transverse network there. They probably contract at intervals when the glands are secreting, and so assist them to discharge their contents.

The connective tissue of the mucous membrane is chiefly adenoid. It is not very evident anywhere except around and between the closed ends of the follicles. In its meshes there are lymph corpuscles. In some cases it is collected into masses that look like solitary glands. But unlike solitary glands proper, they have no envelope. In the stomach of the cat, but not in that of man, there is a clear elastic layer immediately inside the muscularis mucosæ. It is pierced by the muscular bundles that run between the glands.

In the mucous membrane there are many capillaries running parallel with the follicles, and forming a network around their necks. There are also many lymphatics between the glands and in the submucosa.

Gastric juice may be obtained from a dog by means of a gastric fistula. An incision is made in the linea alba and in the wall of the stomach. The lips of the wound in the gastric wall are stitched to the edges of the linea alba, and a silver cannula is introduced and retained in the fistula by a shoulder inside the stomach and another outside the abdomen. When the edges

of the fistula are healed, the gastric juice may be obtained by stimulating the mucous membrane with a feather or with the vapour of ether, or by pieces of sponge introduced through the fistulous opening. The juice has also been obtained from fistulous openings produced by injury in the human subject.

Gastric juice is a sour, watery, almost colourless fluid, sp. gr. 1005. The composition of human gastric juice is as follows:—pepsin, 0·3 per cent.; hydrochloric acid, 0·2 per cent.; various salts, viz., $MgCl_2$, NaCl, KCl, $MgHPO_4$, K_3PO_4, $Fe(PO_4)_2$—0·2 per cent.; and the rest water. In carnivorous animals there is much more acid. The only free acid present in normal gastric juice unmixed with food is hydrochloric acid. During digestion free organic acids, viz., malic, acetic, lactic, and butyric, are liberated from their salts contained in the food. The three acids last mentioned are also sometimes produced in the stomach by fermentation of sugar.

There are two ferments in the gastric juice, viz., *pepsin* and the *milk-curdling ferment*. Pepsin is the chief ferment. It is an albuminoid substance of unknown composition. It is soluble in dilute hydrochloric acid, in dilute alcohol, in water containing a trace of chloroform, and in glycerin. It assists the hydrochloric acid in transforming proteids into peptones. The milk-curdling ferment is produced in comparatively large quantity in the stomach of the calf, but in small quantity in the human stomach.

Secretion of the Juice.—It is not secreted constantly, but only when the glands are stimulated. In the fasting condition, the stomach contains nothing but mucin and saliva. The gastric glands may be stimulated mechanically by a feather or a glass rod. In that case the secretion is local, being confined to the stimulated area and its immediate neighbourhood. Chemical stimulation is much more powerful, and may be effected by the vapour of ether, by alcohol, dilute alkalies, pepper and mustard, and various other substances. The food, however, is the most efficient stimulus, and food which is of semisolid consistence is more stimulating to the glands than fluid food; therefore the food probably acts as a mechanical as well as a chemical stimulus. Painful stimulation of the stomach, severe pain in any part of the body, also febrile conditions, lessen or may even arrest gastric secretion. Some of these facts were ascertained by Beaumont in a case of gastric fistula in a man, and some by observations on the dog.

Formation of the Constituents of the Juice.—In the peptic glands during the early stage of digestion, the adelomorphous cells of the gastric glands become enlarged and very granular. The delomorphous cells also become enlarged but do not become granular. At a later stage, the adelomorphous cells diminish in size owing to a discharge of granules. The granules are probably those of a pepsin or preliminary substance named pepsinogen, which is dur-

ing the secretion transformed into pepsin. In the pyloric glands the cells at the bottom of the glands become more granular during the early stage of digestion, and then lose their granules as secretion proceeds; in that respect, therefore, resembling the adelomorphous cells of the peptic glands. *The pyloric glands secrete pepsin but no acid*, as shown by Heidenhain. He exposed the stomach of a dog and separated its pyloric portion by two incisions. He stitched the left end of the stomach to the pyloric opening of the duodenum, so that the food digested in the stomach might pass on into the duodenum as before. He then closed with stitches the pyloric end of the isolated pyloric portion of the stomach, and he stitched the margins of its cardiac end to the edges of the linea alba, and thus established a fistula in connection with the pyloric portion of the stomach. After some days he stimulated the glands, and collected the secretion with a cannula introduced into the fistulous opening. He found that the secretion from the pyloric portion of the stomach, thus isolated, contained pepsin but no acid. It is alkaline and viscous like the mucus of the stomach generally.

The secretion of the peptic glands is watery, and contains pepsin and hydrochloric acid. The HCl is produced only in that portion of the stomach whose glands contain delomorphous cells. In the fundus of the frog's stomach, the glands have only delomorphous cells, and they produce acid but no

pepsin. The œsophageal glands of the same animal produce pepsin but no acid. They have cells resembling the adelomorphous cells of the peptic glands, but no delomorphous cells. The HCl probably springs from the splitting up of NaCl by the cell protoplasm. Its production must be regarded as resulting from the vital activity of the protoplasm. The liberated alkali enters the blood, and no doubt assumes the form of sodium carbonate. There is always sodium carbonate in the blood, but its amount is increased during the secretion of hydrochloric acid by the gastric glands. Part of it is excreted by the kidneys, and may render the urine neutral or even alkaline in reaction. The greater part, however, is separated from the blood by the pancreas, and is of service in aiding the digestion of proteids in the intestine, as will afterwards be shown.

Nerves of the Stomach.—The stomach receives branches from the sympathetic and pneumogastric nerves, and there are many ganglia in its submucous and muscular coats. The *sympathetic* fibres come from the great splanchnic nerve. They pass to the solar plexus and cœliac ganglia, from which fibres pass to the stomach. The great splanchnic is the vaso-motor nerve of the stomach, pancreas, liver, and intestine. When divided on both sides, there is paralysis of the vessels of these parts, which, however, is only of a temporary character. When the peripheral end of the nerve

is stimulated, there is constriction of vessels in the parts mentioned; there is no secretion of gastric juice. The right pneumogastric nerve gives branches to the posterior surface, the left nerve to the anterior surface, of the stomach. These gastric filaments are certainly motor and sensory, perhaps also secretory for the stomach.

Motor Fibres of the Vagus.—If either vagus be divided, say in the neck, and its lower end stimulated, motion takes place at the cardiac end of the stomach. The movement is not very marked unless the stomach contain food, in which case it may be readily induced. The centres for the movement of the pyloric end and of the greater part of the gastric wall are no doubt in the ganglia in the gastric wall, as is the case with the intestine.

Sensory Fibres of the Vagus.—The vagus is the sensory nerve of the stomach. It contains vaso-inhibitory fibres. When food is introduced into the stomach, there is not only a secretion of gastric juice induced, but also a marked dilatation of blood-vessels in the gastric wall. The vagus is concerned in the vascular dilatation, as may be proved by dividing both vagi during digestion, when it may be seen that the gastric mucous membrane becomes pale. Stimulation of the peripheral end of the divided vagus produces no visible change in the gastric vessels. Stimulation of its central end sometimes gives a negative result; sometimes, however, dilatation of gastric

vessels is visibly produced. The action of the nerve is reflex through the vaso-motor centre in the medulla. But certainly the gastric vessels can be dilated by the introduction of food into the stomach without the intervention of the vagi; for, when the gastric branches have been divided below the diaphragm so that respiration may not be interfered with and the animal may continue to live, it is found that introduction of food into the stomach produces vascular dilatation and secretion as in the normal case. In the latter case the action must be upon a local mechanism.

There is certainly, however, some nervous channel between the brain and the gastric glands. That was conclusively shown by observations made by Richet on a case of gastric fistula in the human subject. The œsophagus was entirely occluded, owing to the swallowing of caustic alkali, and a gastric fistula had to be established, through which food could be introduced into the stomach to keep the individual alive. Richet observed that gastric juice was secreted when sugar or a piece of lemon was placed in the mouth. The effect on the gastric glands may have been reflex, or it may have been due to sensation, and its consequent thoughts; for it was observed that the mere sight of food induced secretion of juice. The vagus is probably the channel of communication between the brain and the gastric glands; yet direct experiments regarding the influence of the vagus have led to equivocal results. Many observers have maintained

that section of the vagi in the neck in the dog interferes with gastric digestion, and may for a time arrest it. Heidenhain, however, has found that when the vagi are divided at the lower end of the œsophagus, so that respiration is not interfered with, the secretion of gastric juice is still called forth when food is introduced into the stomach. He found that division of the sympathetic connections of the stomach, by removing the cœliac ganglia, in addition to division of the vagi in the region just mentioned, also failed to arrest gastric secretion. The effect of stimulating the lower end of the vagus after its division in the neck is also disputed. Fluid sometimes appears in the stomach, but Schiff and Heidenhain maintain that it is the content of the duodenum moved into the stomach by anti-peristaltic action, because bile may sometimes be found in the fluid. Heidenhain watched the gastric mucous membrane of a dog with a speculum introduced through a fistulous opening, and he failed to observe any gastric juice trickle from the follicles during stimulation of the vagus. A like negative result followed stimulation of the sympathetic. Notwithstanding these experiments, however, the fact remains, that the sight of food and the chewing of a lemon when nothing could pass from the mouth to the stomach through the occluded œsophagus in the case observed by Richet, excited gastric secretion. Probably the vagus is the nerve through which the influence passed. The chief

secretory centres, however, are in the ganglia in the gastric wall. The food in the stomach probably excites secretion, principally by acting on a local mechanism. Perhaps the secretory fibres of the vagus merely enable a reflex influence from the mouth and emotional conditions to affect the peripheral secretory centres.

Digestion of Food in the Stomach.

The great action of the gastric juice is on proteids. It converts them into peptones. When compared with albumin, heat and nitric acid coagulate albumin, but do not coagulate peptones; tannic acid and mercuric chloride coagulate both; and, while albumin scarcely diffuses through animal membrane, peptones diffuse readily. Gastric juice can dissolve coagulated proteids and convert all proteids into peptones. The great object of gastric digestion is to render all proteids soluble and diffusible.

Peptic digestion can be readily effected with an artificial juice, containing pepsin 0·3 per cent., HCl 0·3 per cent., in water. A coagulated proteid, such as fibrin, is readily dissolved. Fibrin should, however, be boiled to destroy traces of pepsin derived from the blood.

The functions of the pepsin and the acid may be illustrated by the experiment shown in the following table.

Beaker A.	Beaker B.	Beaker C.
Pepsin, 0·3 %. Water. Fibrin.	HCl 0·2 %. Water. Fibrin.	Pepsin, 0·3 %. HCl, 0·2 %. Water. Fibrin.
All kept at 100° F.		
No change.	Soon becomes acid albumin, viz., syntonin, and this slowly becomes peptone.	Soon becomes peptone.

Pepsin alone is inert. Dilute HCl alone slowly transforms the proteid into peptone. The process is greatly accelerated by adding pepsin to the dilute HCl. The pepsin acts as a ferment; the HCl is used up in the process, as may be proved by adding to the digestive fluid in beaker C more and more fibrin, till no more is dissolved. The addition, then, of pepsin produces no visible effect, but when HCl is added the digestion again goes on. Probably the acid combines with the proteid. An exceedingly small quantity of pepsin can digest a large, but not an unlimited, quantity of proteid. It is probably slowly decomposed by the digestion.

An acid is essential for peptic digestion. The process ends when the juice is neutralized with an alkali. The necessary amount of HCl varies from 0·1 to 7 per cent. HCl is not the only acid with which peptic digestion can be carried on. Lactic

acid, sulphuric and phosphoric acids are all efficient, but not so efficient as HCl. The nature of the transformation of proteids into peptones is not exactly known. Hermann supposes it to be a process of hydration. According to Kühne, it is probably a process of splitting of the proteid molecules, accompanied by hydration; while Hoppe-Seyler considers the principal change to be a linking of an acid to the proteid accompanied by hydration. Several peptones are produced from the different substances, but the differences between them are probably not of great moment. Leucin and tyrosin, two effete matters, are produced in small amount from the decomposition of the peptones. There is also a bitter substance produced.

Casein is first of all coagulated by the gastric juice; the coagulation being due to the acid and to the milk-curdling ferment. The latter, however, can coagulate casein when no acid is present. The casein coagulum is then transformed into soluble peptones by the HCl and pepsin.

Gelatine is converted into a kind of peptone named gelatine-peptone, and sugar. Gelatine, however, is not nearly so nutritious as proteids. When substituted for proteids in the food, partial starvation is the result.

Hyaline cartilage is difficult to digest; it behaves like gelatine. The sarcolemma of muscle and the envelopes of fat cells are soon dissolved. Elastic tissue takes many hours, it may be some days, to

dissolve. Epidermic tissues, nuclei, and mucin are not affected.

Starch is not affected by the gastric juice. Cane-sugar is probably not inverted into glucose or maltose in the stomach. It is, however, inverted by a ferment in the intestinal juice.

Fat is by many said to be unaffected by the gastric juice, but in some cases of dyspepsia, acidity follows the ingestion of much fat. The acidity comes on towards the close of digestion, and appears to result from splitting of neutral fats, and liberation of fatty acids (Roberts).

Cooking renders many foods more palatable. Boiled muscle is more quickly digested than unboiled muscle, because boiling dissolves white fibrous tissue, and allows the gastric juice to reach the sarcous matter more easily. Coagulated albumin, however, is not so quickly digested as raw albumin, as observed by Blondlot in a dog with gastric fistula. He found that 100 grammes raw albumin, beaten to a froth, were digested in three and a half hours, while the same amount of coagulated albumin, finely divided, required five hours to digest it fully.

Acid fermentations of the sugar of the food sometimes occur in the stomach. In some persons they are apt to follow the ingestion of green vegetables, or milk. They are very common in gastric catarrh—where there is excessive secretion of gastric mucus. Lactic acid fermentation is the most common. It is by some attributed to a

ferment in the gastric mucus. However induced, it is in practical medicine important to remember that dilute sulphuric acid prevents lactic acid fermentation. Acetic and butyric fermentations sometimes also occur. Butyric fermentation is accompanied by the development of much CO_2 and H, thus giving rise to flatulence. These fermentations probably result from fungi swallowed with the food, which give rise to fermentations in the stomach under exceptional circumstances. It is important to keep in mind that when these acid fermentations frequently occur in the stomach, the HCl secreted by the peptic glands may come to be deficient, and digestion may be weakened on that account.

Gases in the Stomach.—The stomach always contains the nitrogen of swallowed air. Its oxygen is absorbed. There is always CO_2, most abundant during digestion, and in that case probably derived from the food. As already stated, butyric acid fermentation occasions a rapid development of CO_2 and H. Mental excitement during digestion sometimes produces a rapid development of gas probably owing to some change in the composition of the gastric juice.

Gastric digestion is affected by various conditions. The food should be palatable, readily digestible, moderate in amount, and minutely subdivided by sufficient mastication. It should be taken at regular intervals, for the gastric glands are exhausted by secretion, and require repose for

periods which should be regular in recurrence and in duration. The food must also be thoroughly mingled with a sufficient quantity of normal gastric juice.

The food is constantly moved during digestion by a peristalsis of the gastric wall. The wave of contraction begins at the cardiac orifice, and travels slowly towards the pylorus, carrying with it the food in contact with the mucous membrane, and creating a central return current from the pyloric towards the cardiac end (Brinton). The movement is reflex; its centres being chiefly if not entirely in the gastric ganglia, as those for the peristalsis of the intestine are in the wall of that viscus. Digestion proceeds most favourably in absence of severe exertion, mental or muscular. A condition of bodily quiescence is the most favourable, but not the condition of sleep. Sleep always retards digestion. It is stated by Busch that gastric movements cease during sleep. On the other hand mental exhilaration promotes digestion perhaps by increasing secretion of gastric juices, and possibly also by some favourable influence on gastric movement. In cases of weak digestion, alcohol and various bitter tonics are of service. Probably all act on the nervous system and on gastric glands directly or through their nerves. Alcohol is of special service when indigestible food is taken. Alkalies retard digestion probably by neutralising the acidity of the gastric juice. When undue acidity is developed in the

course of digestion, pure sodium bicarbonate is the most efficient remedy of a temporary character. The *liquor pepticus* prepared by Mr Benger of Manchester, or pepsine, either of them taken with or without dilute HCl, are of much service in weak digestion. Dilute HCl taken alone is often useful, especially in fevers, where the secretion of HCl by the peptic glands is much diminished. Food partly or wholly digested may also be given when the gastric follicles are weak. This subject will, however, be further considered after pancreatic digestion.

Digestion of the Gastric Wall.—When death occurs during digestion, the gastric wall is sometimes found partially digested. The occurrence is most frequently met with in children. The question arises, Why does the gastric juice not attack the wall of the stomach during life? Bernard suggested that it is protected by the epithelium. But after death the epithelium fails to protect it. The epithelium may be scraped away, and the mucous membrane abraded without the exposed tissues becoming digested, provided their vitality is not depressed. But if the vitality of the gastric wall is seriously depressed, *e.g.*, by tying the artery of a small district, or by drinking very hot liquids, digestion of the devitalised tissues take place, and ulcers are formed. It has been suggested that the alkalinity of the blood and lymph keeps the tissues of the stomach from being attacked by the acid of the juice. But in the pancreatic juice there is a ferment which acts on proteids in the

presence of alkali, viz., sodium carbonate, found not only in the blood and lymph, but also in the pancreatic juice; yet the living tissues of the pancreas are not digested.

The food in the stomach is gradually changed into a grey fluid named chyme. Some absorption takes place in the stomach. Very diffusible matters, such as alcohol, pass through the gastric wall. Absorption, however, chiefly takes place in the intestine. The food is retained in the stomach by the contraction of the sphincter of the pylorus. That relaxes at a period varying from one to six hours after food has been taken; the average period is about three hours.

The relaxed sphincter may allow both undigested and digested food to pass into the duodenum. But undigested food may be retained in the stomach for a long time, *e.g.*, elastic tissue may be found in the stomach of a dog several days after it has been swallowed.

Vomiting.

Previous to the act of vomiting there is a rapid flow of saliva, which is probably induced reflexly through the gastric branches of the vagus, at all events when vomiting is induced by the contents of the stomach. When the act of vomiting is just about to occur, a deep inspiration is taken and the glottis is closed, in order that the diaphragm may be pressed down upon the stomach and fixed in that position. The muscles of the abdominal wall

then contract and squeeze the stomach. The part played by the stomach has been disputed. Majendie maintained that it does not contract. Schiff, however, found that shortening of the longitudinal fibres that pass from the œsophagus along the gastric curvatures takes place, and probably there is also some contraction of the general gastric wall. Certainly in normal conditions, portions of imperfectly masticated food are ejected by the stomach, and moved up into the mouth by an antiperistaltic contraction of the œsophagus. The condition is analogous to the act of rumination, and it occurs in some persons to a remarkable extent. The vomited matters are prevented from passing into the nose by contraction of the palato-pharyngei muscles.

The motor nerves concerned in vomiting are the phrenics to the diaphragm, the lumbar and sacral nerves to the abdominal muscles, the œsophageal and gastric branches of the vagus. The nerve centre concerned is in the medulla. The act of vomiting may be excited by disagreeable thoughts, disagreeable odours, and giddiness. It is commonly induced reflexly; it may be by a peculiar excitation of the posterior third of tongue, *e.g.*, by a feather, by the point of a finger, or by an elongated uvula. The afferent nerve in that case is the glossopharyngeal. It may also be induced reflexly from the stomach by emetics, *e.g.*, mustard and hot water, sulphate of zinc, ipecacuan, tartar-emetic. The afferent nerve is

the vagus. Vomiting may also be induced reflexly by the severe stimulation of ordinary sensory nerves, and it is very apt to occur when the sympathetic system is powerfully stimulated, *e.g.*, by renal and biliary calculi and intestinal obstruction.

The Food Appetites.

These are, desire for air, desire for water, and hunger. They are probably all due to a condition of certain tissues—that condition being referable to the state of the blood. The tissue, so to speak, cannot get from the blood the elements which it requires, and therefore a peculiar sensation is produced.

Want of air produces a sensation referred to the region of the chest. It is probably, however, due to a condition of the medulla oblongata, probably to the want of oxygen in it. The air appetite usually becomes so powerful by the end of a minute that it becomes impossible to resist the desire to breathe. The reason is, that the supply of oxygen in the blood and tissues is small, and therefore quickly used up; consequently, before a minute has elapsed, the want of it is so much felt that the sensation results. Death usually supervenes if an individual is deprived of air from three to five minutes.

The sensation of thirst is accompanied by a feeling of dryness of the mouth and throat, *i.e.*, in the region of the fifth and glossopharyngeal nerves. Perhaps the sensation is to some extent due to a

deficiency of water in the nerve terminations in these regions. That idea is supported by the fact, that the application of water to the mucous membrane in these regions can for a time allay the thirst. Only for a short time, however, because the sensation is mainly due to the want of water in the blood. It may be allayed by injecting water into the blood. The thirst disappears most rapidly, however, when the fluid is taken by the mouth, *i.e.*, when it is applied immediately to that region where there is the peculiar sensation of dryness. Ice allays thirst much better than water. Tea without sugar is perhaps the best drink for allaying thirst under ordinary conditions. The want of water, like that of air, causes a disagreeable sensation. The want of water cannot be endured for more than three days; unless it be supplied, delirium sets in, and is followed by death. The drinking of sea-water hastens death.

Hunger is accompanied by a sensation in the gastric region. The sensation of hunger has been ascribed to the empty condition of the stomach, and probably that is so to a certain extent. If pieces of sponge be introduced into the stomach of a dog, through a gastric fistula, it allays the hunger for a short time. But the hunger returns, because it is really due to the want of certain materials in the tissues. The return of the appetite is exhibited by the dog even after the vagi, *i.e.*, the sensory nerves of the stomach, have been divided. No doubt it is due to a peculiar condition of the

nervous system, referable to the state of the blood. The appetite for solid food is at first an agreeable sensation, but soon becomes disagreeable if not satisfied. The appetite is diminished by the emotion of grief or fear, and also by narcotic drugs. The length of time that a person can remain without solid food varies in different cases according to the strength of the individual. From one to three weeks is the limit in most persons, provided water is supplied. It is dangerous to eat much after starvation. The gastric glands are so weak that they are not able to secrete gastric juice, and probably the ganglia in the stomach are so weak that they cannot bring about the necessary movements. Peptonised food ought to be given to a starved individual.

Morbid desires for solid food, water, and air are due to abnormal conditions of the nervous system.

Intestinal Digestion.

The pancreatic juice, bile, and intestinal juice are poured upon the food in the intestine. The grey chyme, which is derived from the stomach, and which passes from the stomach into the duodenum, is gradually changed in the intestine to a milky fluid named chyle.

The Pancreas.

The pancreas is a compound tubular gland. It has a capsule of fibrous tissue which sends in septa

into the interior of the gland, dividing it into lobes, and subdividing the lobes into lobules. There is usually one duct, named the canal of Wirsung. Sometimes there are two ducts. The duct divides, sending a branch to each lobe, which subdivides, and sends a branch to each lobule. The duct is lined by a layer of columnar epithelium, and outside that there is a layer of branching endothelial cells. Outside the basement membrane there is a layer of non-striped muscle arranged in a circular manner, and outside that again there is a fibrous sheath continuous with the general capsule of the gland. In the larger ducts there are mucous glands. The smaller ducts are lined by a somewhat flattened epithelium, and open into the secreting tubules. These branch and form a network. They have an endothelial basement membrane, and inside it a layer of cells, usually columnar. The cells are peculiar in having an outer and inner zone. The outer zone of each cell is striated, owing to the arrangement of the protoplasmic network. The outer part of the cell is not granular. Stains readily with carmine and logwood, and usually contains the nucleus. The inner zone is granular, and is scarcely at all stained by the above dyes.

The inner zone varies according as the cells are resting or secreting. When they are in a resting condition the inner zone is relatively large and very granular. When secretion takes place, the zone becomes smaller owing to the discharge of

granules. There are also in the secreting parts of the gland branched epithelial cells. These are found here and there between the secreting cells. They have been named the *centro-acinous* cells, *i.e.*, cells central in the acinus. Their function is not known.

The pancreatic duct opens at the junction of the middle and lower thirds of the duodenum. In the dog there are two ducts, and these open at a little distance from each other. In the rabbit there are also two ducts (fig. 15). The large one opens 12 to 18 inches below the bile duct. In the human subject the pancreatic and bile ducts open together into the duodenum. They open into a little cavity in the mucous membrane, named Vater's ampulla.

The pancreatic juice may be obtained from a fistula. An opening is made in the linea alba of the dog and a cannula is placed in it, and the secretion collected. It is not secreted constantly. It begins when the food enters the stomach, and the maximum of secretion is attained when the food has been from two to three hours in the stomach. The secretion then falls although the food is still in the stomach. Then it rises again somewhat when the food passes into the duodenum, and the secretion continues while the food is in the small intestine. Probably the pancreas is stimulated reflexly from the gastric mucous membrane and from the duodenal mucous membrane, when the food is in

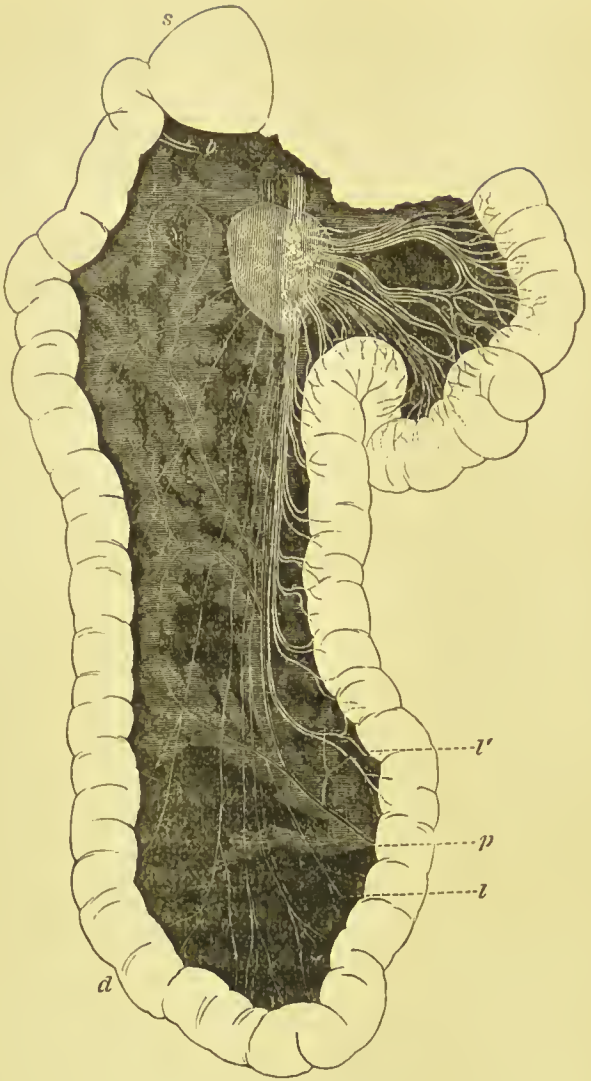


FIG. 15.—Duodenum, pancreas, and lacteals of rabbit; *s*, stomach; *d*, duodenum; *b*, common bile duct; *p*, pancreatic duct; *l*, lymphatics above entrance of pancreatic duct; *l'*, lymphatics below entrance of duct filled with chyle passing to a mesenteric gland (Bernard).

contact with these parts. The nerve mechanism is not known. Probably, however, the vagi are the afferent nerves from the stomach. That idea is supported by the fact that when the vagi are divided secretion may be for a time arrested. When, however, the upper or lower end of the divided vagus is stimulated, no secretion has been observed. Stimulation of the medulla oblongata, however, produces secretion.

The blood-vessels in the gland are much dilated when it secretes. Nothing is known, however, of the secretory nerves, nor of the nerves which dilate the blood-vessels.

Atropia arrests secretion, and no doubt does so by paralysing the secretory nerves. When all the nerves accompanying the pancreatic duct are divided, a paralytic secretion takes place. The gland begins to secrete if it has not been secreting, and it goes on until it is entirely exhausted. We saw that there was a similar paralytic secretion produced in the salivary glands by the division of all their nerves. It is as yet impossible to say what may be the cause of the paralytic secretion.

Characters of the Pancreatic Juice.—It is colourless, viscous, and strongly alkaline, owing to the presence of sodium carbonate. It contains cells resembling salivary corpuscles when the juice is perfectly recent. If, however, the juice stand for some time these cells disappear. No doubt they are digested by the juice. The composition of the pancreatic juice is as follows:—

		Per cent.
Organic matters,	Albumins, . . .	8·2
	Ferments, . . .	
	Leucin, . . .	
Salts, .	Sodium carbonate, .	0·8
	Chlorides of Na and K, .	
	Phosphates of Ca, Mg, Na,	
Water, ...		91

There are two albumins, viz., serum-albumin and an alkali-albumin. The alkali-albumin is a peculiar form of casein. When the juice is heated it coagulates owing to the serum-albumin which it contains.

There are Four Ferments in the Pancreatic Juice.—1. A ferment that splits up neutral fats, named by some *steapsin.*

2. A sugar-forming ferment, named by some *amylopsin.*

3. A peptone-forming ferment, named *trypsin.*

4. A milk-curdling ferment. A watery infusion or an extract of the pancreas made with glycerine which dissolves the ferments may be used for pancreatic digestion. Or the liquor pancreaticus prepared by Mr Benger. The glycerine extract of the pancreas and the liquor pancreaticus contain all the ferments excepting the fat-decomposing ferment.

The action of the pancreatic juice on fat is its great action in digestion. It emulsifies fat. An emulsion is oil in a state of exceedingly fine mechanical subdivision. The emulsification of oil

is not possible unless it be in a fluid which has an attraction for the oil molecules. For example, if we mix oil and water and shake, we no doubt get a slightly milky appearance for a time, but ere long the oil separates from the water, showing that an emulsion has not been formed, because the molecules of the water have no attraction for those of the oil.

But if we take oil and water and some albumin and shake the mixture, an emulsion is obtained which, though permanent, is, however, not very marked. Pancreatic juice contains albumin, and that probably is of some service in emulsifying oil. It is, however, difficult to know how long the albumin remains in the juice. It is no doubt in time digested by the trypsin of the juice.

The presence of sodium carbonate is of great service in emulsifying oil, and appears to be the great cause of emulsification. The molecules of the alkali have an attraction for those of the oil. Part of the oil is decomposed into glycerine and fatty acids. The latter unite with the alkali to form soaps, and the presence of soaps assists emulsification. In the pancreatic juice the effect of the sodium carbonate is assisted by the ferment in the juice that decomposes fat. The ferment splits neutral fats into glycerine and fatty acids, the latter uniting with soda to form soaps. The decomposition of the fats of the food, and the formation of soaps, does not, however, take place to a large extent. Most of the fat is simply

emulsified. The object of emulsification is to enable the oil to pass through the wall of the intestine. It has to be very finely subdivided before it can pass through the interstitial matter between the epithelial cells lining the intestine into the lacteals. The bile scarcely produces any emulsification of the fat, so that the lymphatics below the entrance of the bile duct in the rabbit (fig. 15, *l*) remain clear. But below the entrance of the pancreatic juice (*l'*) the lymphatics present a milky appearance, owing to the absorbed fat, showing that the pancreatic juice is of great service in assisting the absorption of fat. When the flow of the juice into the intestine is prevented by a cancerous tumour or by some other cause, the fat of the food appears in the dejections, and the individual becomes starved so far as regards fatty matter.

The Action of Pancreatic Juice on Starch.—It converts starch into maltose as the saliva does, and it is in that respect even more powerful than the saliva.

The Action of Pancreatic Juice on Proteids.—This is due to the ferment *trypsin*, assisted by the sodium carbonate,—the alkali of the juice. Trypsin is of unknown composition. It differs from the pepsin remarkably in the fact that it is of itself able to transform proteids into peptones. Pepsin cannot do so alone, but must be assisted by an acid. Trypsin cannot act when an acid is present. The fluid must be alkaline, and it is

assisted by the presence of the alkali. The part which the alkali plays is not understood. It has been suggested that, like the acid of the gastric juice, the alkali of the pancreatic juice combines with the proteids to form alkali-albumin. That has not been definitely shown. In the digestion of fibrin, at all events, there is really no sufficient evidence of any such effect. The fibrin does not to any remarkable extent swell up as it does in the gastric juice. It becomes slowly eroded and dissolved. In the case of the gastric juice the *pepsin assists* HCl in producing peptones; in the case of the pancreatic juice the *alkali assists the ferment* in producing the peptones from the proteid. Gastric digestion chiefly ends in the production of peptones, but little of the peptones being transformed into effete matters. On the other hand, tryptic digestion, if it be allowed to continue for a long time, not only produces peptones, but it can split up much of the peptone into leucin and tyrosin and other effete substances. Leucin is amido-caproic acid, of which the formula is $C_6H_{10}(NH_2)O(OH)$. Tyrosin is an amido-acid of unknown constitution, $C_9H_{11}NO_3$. The trypsin of the pancreatic juice no doubt acts on proteids that have escaped the action of the gastric juice. The pancreatic juice, however, cannot act until the acid of the chyme has been entirely neutralised by the sodium carbonate of the pancreatic juice and of the intestinal juice.

The Use of Digested Food.

Digestion may be assisted by giving pepsin or liquor pepticus, with or without dilute hydrochloric acid.

Some have recommended that an extract of the pancreas should be given along with the food to assist the digestion of fat. Dr Roberts of Manchester has pointed out that such a proposal is futile, because the pancreatic ferments are destroyed by the prolonged action of the gastric juice.

It is of great service in some cases of weak digestion to give peptonised food. It may be prepared either by peptic or by tryptic digestion. Peptic digestion, however, is not suitable for peptonising food out of the stomach, because it removes the agreeable taste and odour, and so renders it unpalatable, a bitter substance being always produced in quantity sufficient to render it disagreeable. When food is peptonised by tryptic digestion, it is much more agreeable.

Peptonised milk is made as follows:—A pint of milk is heated to a temperature that can be borne by the mouth (about 100° F.), a tablespoonful of liquor pancreaticus, and 20 grains of sodium bicarbonate, are added and thoroughly mixed with it, and the mixture is kept at the above temperature for two hours. It is then boiled for a few minutes to arrest further digestion. Digested milk, however, is bitter and not very palatable. Most

animal proteids are rendered bitter by pancreatic digestion, but not so bitter as by peptic digestion. *Vegetable proteids* are not rendered bitter (Roberts).

Peptonised gruel contains the nutritive elements of oatmeal, and is very nutritious. It is sweet, and has no trace of bitterness, but it is not very agreeable to the palate.

Peptonised milk-gruel is much preferred by invalids, and is prepared as follows :—Half a pint of thick oatmeal gruel is prepared in the usual manner, and boiled for a few minutes. An equal volume of cold milk is then added to it, and 20 grains of sodium bicarbonate and a tablespoonful of liquor pancreaticus. The temperature of the mixture will be about 120° F. It is placed under a tea-cosey and kept for two hours. Digestion is then stopped by boiling for a few minutes (Roberts). The bitterness of the peptonised milk is concealed by the sweetness of the gruel. That preparation is found of great service in practical medicine. The strength may be maintained with it for weeks.

Peptonised beef-tea is also a preparation of much value, and is prepared as follows (Roberts) :—Half a pound of minced beef, half a pint of cold water, and 20 grains of sodium bicarbonate, are mixed together, and allowed to simmer gently for an hour and a half, and then cooled to about 100° F. A tablespoonful of liquor pancreaticus is then added, and the mixture is kept at about 100° F. for two hours ; it is then strained and boiled for five

minutes. It contains 4½ per cent. of organic matter, and is therefore very nutritious, and it is also palatable.

It is preferable to prepare digested food shortly before it is taken, rather than to use the preparations of digested food sold in the market.

The Liver.

The Structure of the Liver.

The liver is composed of lobules of somewhat oblong shape, and about $\frac{1}{15}$ inch in diameter.

Connective Tissue.—A thin general capsule of fibrous tissue envelops the liver, and is continuous with the fibrous layer of the peritoneum. The capsule sends into the interior, sheaths around the blood-vessels and bile ducts. *The capsule of Glisson* is the sheath around the portal vein, hepatic artery, and hepatic ducts, that enter the liver at the portal fissure. It accompanies the vessels between the lobules, but does not enter the lobules. At the general surface of the liver it joins the general capsule by thin septa.

A thin sheath of fibrous tissue accompanies the hepatic vein from the posterior border of the liver, and extends to the radicles of that vein.

Blood-vessels.—*The portal vein* conveys to the liver blood which has passed through the vessels of the stomach, intestine, pancreas, and spleen. It enters the liver by the portal fissure, subdivides and passes between the lobules as the *interlobular veins*. These open into the lobular capillaries at the periphery of the lobules. The blood passes through the lobular capillary network to the *intra-*

lobular veins, which arise in the centres of the lobules, and are the radicles of the *hepatic vein*. The intralobular veins of several lobules join to form the *sublobular* veins. These again join to form the larger branches of the hepatic vein, which leaves the liver at its posterior margin.

The branches of the portal vein do not anastomose with each other, nor do those of the hepatic vein. The blood entering the liver by the portal vein all passes through the venous capillary network in each lobule, and then leaves the liver by the hepatic vein.

The hepatic artery enters the liver by the portal fissure. It gives off branches that accompany the portal vein and pass with it between the lobules. The branches of the artery anastomose with each other. The hepatic arterioles end in capillaries that ramify in the capsule on the general surface of the liver, in the capsule of Glisson, and in the coats of the larger vessels and bile ducts. The capillaries around the larger vessels in the portal canals pour their blood into small veins that accompany the hepatic artery and open into the interlobular branches of the portal vein. These veins have been named the internal rootlets of the portal vein. The interlobular capillaries of the hepatic artery transmit their blood directly into the venous capillaries at the periphery of the lobules. Johannes Müller described small branches of the hepatic artery, passing into the lobules, and opening into the venous capillaries about midway

between the circumference and the centre of the lobule; but this, although supported by Chrzonszczewsky, appears to be erroneous.

The blood of the hepatic artery passes through two sets of capillaries—the arterial capillaries outside the lobules, and the venous capillaries inside the lobules.

Hepatic cells are of comparatively large size (30 μ). They are polyhedral, nucleated, with a close intercellular network and a thin envelope (Haycraft). The cells are arranged as a network, with a network of blood-capillaries and a network of bile-capillaries between them. There are three networks in each lobule :—(1) a network of hepatic cells; (2) a blood-capillary network; (3) a bile-capillary network.

Bile Ducts.—The common bile duct which opens into the duodenum, when traced backwards, divides into the cystic duct for the gall-bladder and the common hepatic duct. The latter divides into the right and left hepatic ducts. Before entering the liver, the left hepatic duct gives off aberrant ducts that ramify in the longitudinal fissure, and in the left lateral ligament of the liver. The hepatic ducts enter by the portal fissure, and accompany the portal vein between the lobules. The *interlobular ducts* give off small branches, named the *intermediate ducts,* which enter the periphery of the lobules for a very short distance, and then open into the bile-capillaries.

The larger ducts and interlobular ducts have a

basement membrane lined by a layer of ordinary columnar epithelium with chalice cells here and there. There is a circular layer of non-striped muscle outside the basement membrane. The larger ducts have mucous glands in their walls, by which most of the mucin contained in the bile is secreted. The gall-bladder has a structure similar to that of the larger bile ducts.[+] The intermediate ducts have no muscular fibres, and their lining epithelium is either cubical or flattened.

Origin of the Bile Ducts.—According to Beale, the intermediate ducts open into a network of branching tubules composed of a basement membrane lined by hepatic cells, the hepatic cells merely replacing the epithelium of the ducts.

The only point disputed is the existence of a basement membrane enclosing the hepatic cells, and therefore existing between them and the blood-capillaries. It was demonstrated by Beale in the pig's liver. It can be seen in the liver of the child, but not in that of the adult. As age advances the membrane either disappears or becomes inseparable from the walls of the blood-capillaries.

Bile-Capillaries.—The channel of the intermediate bile ducts is continued into a network of fine passages between the hepatic cells, viz., the bile-capillaries. They are very evident in the liver of the snake, after injection with 2 per cent. solution of soluble prussian blue (Hering). They may also be demonstrated by the same process in the liver of the rabbit and in other animals. The

bile-capillaries are never near the blood-vessels; there is always a part of a hepatic cell between the two sets of capillaries. There appear to be some spaces between adjacent hepatic cells. There is no evidence that they have a special envelope as Chrzonszczewsky maintained.

The bile-capillaries may also be demonstrated by a method of natural injection (Chrzonszczewsky). A solution of sulphindigotate of sodium, commonly named indigo-carmine, is injected into a systemic vein of the rabbit; or it may be injected into the subcutaneous tissue of the frog, from which, through the lymphatics, it finds its way into the systemic circulation. The substance is of a blue colour, and is gradually excreted from the blood by the liver and the kidneys. The hepatic cells abstract it from the blood and move it into the bile-capillaries, by which it flows away. If the animal be killed at a suitable interval after the injection, the bile-capillaries are found to be blue. By this method of injection it has been shown, in the liver of the frog, that there are minute vacuoles in the hepatic cells, from which fine channels pass to the bile-capillaries at the periphery of the cells.

The lymphatics of the liver are numerous in the capsule of Glisson, in which many of them take origin. They may be traced into the lobules, in which they originate in a manner not yet fully known.

The nerves of the liver are branches of the

sympathetic, derived from the solar plexus, and branches of the left pneumogastric. They accompany the vessels in the portal canals, and have ganglia upon them at intervals. Their mode of termination is unknown.

The Functions of the Liver.

The functions of the liver are not fully known. It has, however, two well-pronounced functions—(1) to secrete bile; (2) to secrete glycogen. The bile and the glycogen are both produced in the hepatic cells. The bile passes to the bile ducts, and thence to the intestinal canal. The glycogen in some form or other leaves the liver by the hepatic vein.

Biliary Function of the Liver.

The bile is viscid, bitter, neutral, or slightly alkaline. Human bile is yellowish-brown, that of the herbivora is green.

Composition of Human Bile.

Water, . . .	85·92 per cent.
Salts of bile acids, .	9·14 „
Fat, ...	0·92 „
Cholesterin, . . .	0·26 „
Mucin, Pigments, . .	2·98 „
Inorganic salts, .	0·78 „

Traces of Leucin, Tyrosin, Urea, Xanthin, Hypoxanthin.

The viscidity of bile is due to mucin, secreted by mucous glands in the larger bile ducts and gall-bladder, and by chalice cells in the ducts. The slight alkalinity of bile is due to alkaline phosphates and to soda salts of the bile acids. Its bitterness is due to the bile acids.

Bile Acids.—There are two bile acids, both combined with soda, viz., taurocholic acid, $C_{26}H_{45}NSO_7$ and glycocholic acid, $C_{26}H_{43}NO_6$. Taurocholic acid is the chief one in human bile. It contains sulphur. The sulphur of broken down proteids is excreted by the liver in taurocholic acid, and by the kidney oxidised into sulphuric acid. When boiled with dilute mineral acid, each bile acid takes up a molecule of water, and then splits up into two substances. Glycocholic acid splits into glycocine and cholic or cholalic acid ; thus—

Glycocholic acid,
$$C_{26}H_{43}NO_6 + H_2O =$$
Glycocine, $C_2H_5NO_2$. + Cholic acid, $C_{24}H_{40}O_5$.

Taurocholic acid splits into taurin and cholic acid ; thus—

Taurocholic acid,
$$C_{26}H_{45}NSO_7 + H_2O =$$
Taurin, $C_2H_7NSO_3$ + Cholic acid, $C_{24}H_{40}O_5$.

Both bile acids therefore consist of a non-azotised acid united to an azotised substance. Glycocine is amido-acetic acid, that is, acetic acid with an

atom of H replaced by a molecule of amidogen (NH_2). Taurin is amido-ethyl-sulphonic acid, that is, ethyl-sulphonic acid in which an atom of H has been replaced by a molecule of amidogen (see author's *Text-Book*, p. 38).

The bile acids are believed to be produced in the liver, because they cannot be found in normal blood ; nor do they appear in the blood after the liver has been excised. The liver may be excised in the frog without a fatal result. Several observers have performed the experiment, and have found no bile acids appear in the blood. But if the common bile duct be tied in the frog, the bile secreted by the liver is absorbed from the bile ducts, and enters the general circulation. In that case, bile acids can be detected in the blood.

The bile acids are believed to be produced from proteids, because they both contain nitrogen, and taurocholic acid also contains sulphur, and when the food is rich in proteids the production of bile acids is increased.

Both bile acids give a characteristic reaction with cane-sugar and sulphuric acid. If a few drops of syrup are added to bile in a test glass, and ordinary sulphuric acid slowly poured down the side of the vessel, a violet colour appears at the junction of the acid with the bile. That is Pettenkofer's test for the bile acids. The test is apt to fail when much water is present, *e.g.*, in the urine. In that case, strips of white bibulous paper are dipped in the mixture of the fluid with

the syrup, and are then allowed to dry; a drop of strong sulphuric acid is then allowed to fall on the paper, and a violet circle appears around it if either bile acid be present.

Bile Pigments.—There is one primary pigment, the red pigment of the bile, viz., Bilirubin, $C_{32}H_{36}N_4O_6$. It is readily convertible into a green pigment, Biliverdin, by simple oxidation. Thus—

$$\text{Bilirubin, } C_{32}H_{36}N_4O_6 + O_2 = \text{Biliverdin } C_{32}H_{36}N_4O_8.$$

This change happens with simple exposure to the air, but nitric acid, containing nitrous acid, effects it much more rapidly. A play of colours follows the addition of the acid. The first colour to appear is green, due to the production of Biliverdin; the green then changes to blue, owing to the production of Bilicyanin; the blue then gives place to a red colour, due to Cholètelin; all of these being successive oxidation stages of Bilirubin. After a time the Choletelin disappears, and all colour is lost. That is Gmelin's test for bile-pigment. It may be done on a white plate or in a test-tube. In the latter, the tube is inclined, and the acid is cautiously poured down the side of the tube, so that it may form a layer at the bottom. The different colours then successively appear, giving rise to distinct zones, the green zone being above the others, as that indicates the first stage of the oxidation.

Source of the Bile-Pigment.—All are agreed that it is derived from hæmoglobin, (1) because the

pigment hæmatoidin, produced in old extravasations of blood, very closely resembles—is indeed probably identical with—Bilirubin. Both form mahogany-coloured crystals of similar shape; both give a play of colours when nitric, containing nitrous, acid is added. (2) When a solution of hæmoglobin is injected into the blood-vessels, *e.g.*, of a dog, the pigment in the bile is increased to, it may be, twenty times the normal amount.

Coloured blood-corpuscles are broken down in the spleen, and the liberated blood-pigment passes, in the splenic vein, to the liver, and is there transformed into bile-pigment, and excreted. The idea is also entertained by some, that, in the liver itself, a destruction of coloured corpuscles takes place to some extent. The bile-pigment, however, has a far simpler composition than hæmoglobin, and it contains no iron. The iron of the hæmoglobin, however, is excreted by the liver, and is found in the ash of the bile.

It is disputed whether or not the bile-pigment is produced in the liver, or preformed in the blood, and merely abstracted from the blood by the liver. Those who support the idea that it is preformed in the blood adduce the following facts:—(1) That hæmatoidin is produced from blood-pigment without the aid of the liver; (2) that the injection of a solution of hæmoglobin into the blood-vessels is followed, not merely by increased excretion of bile-pigment by the liver, but by excretion of bile-pigment by the kidney. If that be so, it would

go very far to show that the liver is not essential for the production of bile-pigment; but Kühne has not been able to confirm that observation. He finds, however, that if some solution of bile-acids be injected into the blood-vessels along with the solution of hæmoglobin, bile-pigment abundantly appears in the urine. How the injection of bile-acids along with the hæmoglobin causes bile-pigment to appear in the urine is not yet ascertained.

Again, other observers have found, that when coloured corpuscles are broken down in the blood by injecting water, or by inhalation of ether or chloroform, or by injection of phosphoric acid, bile-pigment appears in the urine. There is another fact which, at first sight, appears to support this idea that the bile-pigment is preformed in the blood. In the ordinary condition of biliousness, the skin, the sclerotic, and tongue become yellow, as if bile-pigment were in the blood. The condition appears to depend on defective activity of the liver, for it may certainly be cured by giving substances such as iridin and euonymin, which stimulate the liver to secrete more bile. The inference is, that the bilious colour of the tongue and other parts is cured by causing the liver more efficiently to withdraw bile-pigment from the blood. Caution is needed however, in coming to a conclusion on this point, because the condition of biliousness might be really not due to defective activity of the liver, but to a catarrhal or some

other condition of the bile ducts, impeding the exit of the secreted bile, and so causing its absorption into the blood.

On the other hand, the supporters of the theory that bile-pigment is not preformed in the blood, but produced in the liver, quote the following facts:—When the liver is excised, bile-pigment ought to accumulate in the blood or be excreted in the urine, if it is preformed in the blood; but bile-pigment has not been detected either in the blood or in the urine under those circumstances. Further, Frerichs relates a case where, in the human subject, the liver was disorganised by fatty degeneration. It secreted no bile; the fœcal matters were devoid of bile-pigment; the gall-bladder only contained mucus; there was no jaundice of the skin; no bile-pigment and no bile-acids were found in the blood or in the urine. That observation is opposed to the idea that the bile-pigment is preformed in the blood, or that it may be produced in the blood when the function of the liver is suspended. The question must therefore be regarded as still unsettled.

Cholesterin is another important constituent of the bile. It is an alcohol of unknown constitution, $C_{26}H_{43}(OH)$. It is the only free alcohol in the body. It is insoluble in water; but it is kept in solution in the bile by the salts of the bile acids. Sometimes it is precipitated in the bile, and produces gall-stones. It is abstracted from the blood by the liver. Whether or not it is also produced

in the liver is doubtful. It is abundantly found in the white matter of nerve tissue, and in small quantity in protoplasm[x] generally. The liver is the only channel through which it is excreted.

The fats of the bile are the ordinary neutral fats. There is also a small amount of Lecithin.

There are no proteids, and no cells, excepting only an occasional cell detached from the ducts.

The inorganic solids are chiefly alkaline chlorides, alkaline phosphates, and calcic phosphates. There is also iron; in what state of combination has not been pointed out, but it is in sufficient quantity to give a rust-colour to the ash of the bile.

Secretion of Bile.

The secretion of bile takes place constantly, slowly during fasting, rapidly during digestion. The bile may be collected from a biliary fistula established in the following manner:—An incision is made in the linea alba; the common bile duct is secured, care being taken to injure as little as possible neighbouring parts and nerves going to the liver. A glass cannula with a shoulder is introduced into the duct and tied in it with a ligature. The cannula is made of a length and shape suitable for conveying the bile from the abdominal cavity to a glass measure placed near the animal. The gall-bladder is squeezed in order to fill the cannula with bile, and a small clamp is

placed upon the cystic duct to prevent any bile from passing back into the gall-bladder. The wound in the abdominal wall is then closed, and the secretion collected and measured. The animal can be anæsthetised with ether and chloroform when no observation is to be made upon the action of any drug upon the biliary secretion; but as these substances stimulate the liver, their use is inadmissible when observations upon the amount of bile secreted are to be made. In that case the animal requires to be kept perfectly still by the injection, at intervals, of small quantities of curara into the jugular vein; and, as the voluntary motor nerves of the body generally are paralysed, the animal must be kept alive by artificial respiration. The curara does not appear to affect the secretion of bile. The dog is the most suitable animal for observations of this nature; and if one desire to examine the secretion during a state of fasting, sixteen or seventeen hours should elapse between the last meal and the performance of the experiment under the conditions above mentioned. If the experiment is begun about sixteen hours after a full meal of lean meat has been given, and if care be taken to trouble the hepatic nerves as little as possible during the operation for establishing the fistula, it is generally found that the secretion of bile remains fairly constant during the first five or six hours of the experiment, and then gradually falls, owing either to exhaustion of the liver or to deficiency of the materials for the

production of bile. The composition of the bile, however, remains the same.

The bile is secreted at a very low pressure; in that respect, therefore, differing remarkably from the secretion of saliva. In the cat, the pressure of the secretion does not sustain more than from $\frac{1}{2}$ to $\frac{3}{4}$ inch of mercury. In consequence of this low pressure the outflow of bile is easily obstructed, *e.g.*, by catarrhal swelling of the bile ducts, or by gall-stones. The obstructed bile passes by the lymphatics into the general circulation, and produces jaundice.

The amount of bile secreted in twenty-four hours was measured by Dr Murchison in a case of biliary fistula in the human subject, in which the whole bile was discharged from an opening in the fundus of the gall-bladder; and he found it to be about 40 oz. The amount secreted daily varies; the food is the principal cause of the variation. The amount secreted is always greatly lowered by starvation. Most is secreted when the food is rich in proteids. A diet of liver given to a dog is followed by a large secretion. In the dog also, more bile is secreted on an animal diet than on a vegetable diet; a diet of lean meat with a little fat gives a large secretion in that animal a diet of pure fat is followed by a very small secretion.

Soon after the introduction of the food into the stomach, the biliary secretion rises, and attains its maximum between the fourth and eighth hours

of digestion, that is to say, when the food is in the small intestine. One might be disposed to ascribe the influence of the food to (1) *a reflex nervous effect* proceeding from the gastric and duodenal mucous membranes. But when the mucous membrane of the stomach or duodenum is irritated by such substances as strong alcohol or gamboge, the secretion of the bile is not augmented. (2) The increased secretion might be ascribed to an increased stream of blood through the portal vein, resulting from dilatation of the gastric and intestinal vessels. Probably, however, that is not an important cause of it, for an intestinal irritant, such as gamboge, occasions a very great dilatation of intestinal vessels, and yet the increased stream of blood through the portal vein does not increase the biliary secretion. (3) Probably the chief cause of increased bile secretion after food is a direct excitement of the hepatic cells by substances of the food conveyed to the liver by the portal vein. The increased blood stream in the portal vein no doubt assists when there is a disposition in the hepatic cells to greater activity.

There has been much dispute regarding the influence of the blood of the portal vein and that of the hepatic artery upon bile secretion. Ligature of either vessel lessens the secretion; the diminution is most marked when the portal vein is tied.

Nothing is definitely known regarding the influence of nerves on bile secretion, but if nerves are implicated, they probably belong to the

sympathetic system, because atropia does not arrest—does not, indeed, appear to affect bile secretion. But we have seen that atropia paralyses the filaments of the cerebro-spinal nerves presiding over the secretion of the saliva, while it does not paralyse the secretory fibres belonging to the sympathetic supplied to these glands. Atropia also paralyses the cerebro-spinal nerves presiding over the mammary glands, and the sweat glands. Therefore it is probable that, as atropia does not arrest or diminish the secretion of bile, it is not due to the activity of the cerebro-spinal nerve fibres that pass to the liver, and which, as before stated, belong to the pneumogastric nerve. There is reason for believing that the activity of the liver becomes depressed by conditions which exhaust or depress the action of the nervous system,—such as severe study, deficient sleep, and so on.

The Flow of the Bile into the Intestine.—Although the bile is secreted constantly, it does not usually flow into the duodenum when that viscus contains no food. Perhaps the oblique passage of the common bile duct through the wall of the duodenum offers some resistance to the biliary flow, which is only overcome by a contraction of the muscular fibres of the gall-bladder and larger bile ducts; or more probably, during the intervals of digestion there may be a contraction of muscular fibres at the opening of the common bile duct, preventing the outflow of the bile. There is,

however, no evidence of any definite muscular sphincter at the orifice. The bile accumulates in the gall-bladder and bile ducts during the intervals of digestion, and flows into the intestine when the chyme has poured into it. Before digestion, the gall-bladder is tense and filled with bile; when digestion is over it is lax, and contains much less bile. Bernard observed that a reflex contraction of the gall-bladder is induced by stimulating the duodenal mucous membrane by an acid fluid. The chyme is acid and probably effects the same result. In considering the flow of the bile, two mechanisms must constantly be kept in view:—(1) *The bile secreting mechanism*, viz., the hepatic cells; (2) *The bile expelling mechanism*, viz., the muscular fibres of the gall-bladder and bile ducts. The former is always active—much less so, however, during fasting than during digestion. The latter is reflexly thrown into activity when the acid chyme is passing through the duodenum. Probably muscular exercise, when it entails powerful contraction of the diaphragm and at the same time powerful contraction of the abdominal muscles, occasions a flow of bile into the intestine, by mechanically compressing the liver and gall-bladder. At all events in a dog, with the common bile duct tied, and a permanent fistulous opening in the fundus of the gall-bladder, it may be seen that the bile rapidly flows from the fistula when the animal is allowed to run about, and so to squeeze the liver and express its bile. The liver

virtually resembles a sponge with many canals full of fluid; hence the biliary flow when it is compressed.

Destiny of the Bile.

I. It plays a part in Digestion.
II. Part of it is Excreted.
III. Part of it is Absorbed.

I. *Its Function in Digestion.*—(1) *It has a slight power of emulsifying fat.* When some bile is added to oil and water and the mixture shaken and allowed to stand for some hours, it is found that a very slight emulsion of a part of the oil has been produced, there being a thin zone of emulsion at the junction of the water with the superjacent oil. The emulsifying power of the bile, however, is not nearly so great as that of the pancreatic juice. Bernard's observation on the intestinal lymphatics of the rabbit, below the entrance of the common bile duct, and below the entrance of the pancreatic duct, showed that when bile alone was mingled with the food, no fat appeared to be absorbed, but after the pancreatic juice was added, fat was quickly absorbed and rendered the contents of the lymphatics milky—lacteals. It must not, however, be concluded from that observation, that the bile does not assist the absorption of fat; on the contrary, it has been observed in man and animals, that if bile does not enter the

intestine, fat appears in the dejections. The bile and pancreatic juice acting together, therefore, appear to accomplish more than the pancreatic juice can do alone. This, however, may be because:—

2. *The Bile stimulates the Villi to contraction.*—The contraction of the villi can be seen under the microscope when bile is allowed to run over them in a piece of living intestine. The contraction of the villi so induced must be reflex, the stimulation induced by contact of the bile with the mucous membrane, passing through afferent nerve-fibres probably to the ganglia in the submucous coat, and from them to the muscular fibres of the villi —which are arranged longitudinally, and which by their contraction shorten the villus, and so expel the fat absorbed into the lacteal vessel situated in its centre. The fatty matter or chyle is thus driven to the general lacteals of the intestine, and its return is prevented by their valves. Thus the bile, by exciting what may be termed a pumping action in the villi, doubtless facilitates the absorption of fat by them.

3. *The Bile reflexly stimulates the muscular coat of the intestine to contraction,* and is thus of service in promoting the downward movement of the intestinal contents. The bile is, so to speak, a *natural purgative.* Its diminished secretion is a cause of constipation.

4. *The Bile is to some extent an Antiseptic.*—It probably prevents putrefactive decomposition of

the contents throughout the greater part of the small intestine. It is observed in cases of jaundice, when the bile is prevented from entering the intestine, that decomposition of the intestinal contents takes place to a much greater extent than under normal circumstances. In the large intestine, however, and in the lower part of the small intestine, the bile is no longer able to prevent decomposition, probably because it has itself undergone important changes, presently to be detailed.

II. *Part of the Bile is Excreted.*—In the child before birth, bile is secreted by the liver, and passes into the intestine; its solids accumulate there and form the excrement termed *meconium*. The bile, at that time, can play no part in digestion, for no digestion takes place before birth. The other glands that secrete into the alimentary canal are inactive before birth, but the liver secretes, because in its biliary function it is an organ of excretion, although, as we have seen, the excretion is of use in digestion.

The cholesterin of the bile is excreted in the dejections. According to Austin Flint, it is transformed into a closely allied substance, named by him stercorin.

The *bile pigment* is entirely excreted. It is converted into a pigment, hydrobilirubin, by hydration and reduction: a molecule of bilirubin takes up four molecules of water and loses three atoms of

oxygen and becomes a molecule of hydrobilirubin; thus—

Bilirubin. Hydrobilirubin.

$$C_{32}H_{36}N_4O_6 + 4H_2O - O_3 = C_{32}H_{44}N_4O_7.$$

Hydrobilirubin can be produced from bile artificially by putrefactive ferments, and by reducing agents, such as sodium amalgam. An identical substance, named *urobilin*, is found in the urine. Nothing, however, is definitely known of the relation of the hydrobilirubin produced in the intestine, to the urobilin excreted by the kidneys. It is not known where the urobilin of the urine is produced. Some, however, are inclined to suppose that it is absorbed from the intestinal canal, passes into the general circulation, and is excreted by the kidney. That, however, has not been definitely shown.

Bile Acids.—In the intestine glycocholic acid is split up into glycocine and cholic acid, while tauro-cholic acid is split up into taurin and cholic acid. Cholic acid is found in the fœcal matters; taurin is found there only in small quantity. Taurin contains practically all the sulphur of the bile; and only about one-eighth of the sulphur secreted by the liver in twenty-four hours is found in the dejections during the same period. Therefore, about seven-eighths of the sulphur of the bile must be reabsorbed (Bidder and Schmidt). What becomes of the glycocine is not exactly known. Perhaps it is wholly or in part reabsorbed.

III. *Part of the Bile is Reabsorbed.*—It has just been stated that about seven-eighths of the sulphur contained in the taurocholic acid of the bile is reabsorbed. It has not been shown that the taurin which contains it is reabsorbed as such. The sulphur-containing substance, whatever it be, probably passes from the intestine into the radicles of the portal vein, and probably on passing through the liver it is seized by the hepatic cells, and contributes to the production of taurocholic acid in them. That idea is supported by the fact, that when bile is injected into the small intestine of a dog with a biliary fistula during a condition of fasting, an increased secretion of bile ensues. The amount of bile injected requires, however, to be considerable—about half an ounce. It should also be stated in this relation, that various matters injected into the intestine, *e.g.*, the colouring matter of rhubarb and senna, and mercuric chloride, &c., are absorbed, pass to the liver, are excreted by it and found in the bile. Emaciation may supervene if bile is prevented from entering the intestine. Probably the cause is twofold,—(1) diminished absorption of fat; (2) loss of the sulphur-containing substance normally absorbed from the intestine. Perhaps in consequence of this loss, there is a greater destruction of proteids in the liver to supply the materials for producing bile acids. In the dog, however, the emaciation may be prevented in most instances by giving a larger amount of food, especially food containing *liver*.

Physiological Actions of Drugs on the Bile-Secreting Mechanism.

Perhaps no subject in therapeutics has gained so much from experiments on animals as the actions of drugs on the secretion of bile. Observations conducted on the human subject yielded knowledge of an indefinite character, and which, therefore, gave rise to constant discussion. The flow of bile from the human liver is commonly estimated by the necessarily rough and inaccurate method of observing the colour of the dejections. It is impossible by that method to detect slight variations which may occur in the secretion of bile, and when it happens that a substance such as rhubarb gives of itself a bilious colour to the dejections, it is difficult to say whether or not it stimulates the liver; yet by another method of research it can be shown that rhubarb certainly increases the secretion of bile, where the substance, as in the case of sodium sulphate, stimulates the intestinal glands and thus occasions copious dejections of a watery character, whereby their colour is diluted, the physician has found it difficult to say whether or not there is a variation in the quantity of bile discharged; yet by another method it can be shown that this substance certainly stimulates the liver as well as the intestinal glands. Again, in the case of such substances as magnesium sulphate and castor oil, which stimulate the intestinal glands but not the

liver, the physician, although he certainly did not suppose that they increase the flow of bile, nevertheless failed to observe the fact—which may be shown by another method—that *they diminish the production of bile.* Again, when a substance excites the liver to produce more bile, but does not excite the intestinal glands to pour forth their watery secretion, and as it were wash out the bile discharged into the canal, the clinical observer has in the case of benzoic acid and its compounds, sodium salicylate, and other substances, failed to observe that they increase the flow of the bile. But again, even in the case of substances which certainly increase the flow of the bile, the clinical observer is unable to say whether or not they actually stimulate the hepatic cells to produce more bile, or merely excite the muscular fibres of the gall-bladder and bile duct to expel their contents. Yet rational medicine requires that the first of these questions at all events shall receive a definite answer.

The difficulties that prevent the attainment of definite knowledge as regards the human subject, may be overcome by making biliary fistulæ in animals, and measuring the bile secreted before and after the administration of any drug. That method has not only the advantage of substituting *exact measurement* for superficial observation, which, from the peculiarity of the case, must always be merely approximative; it has also the advantage of eliminating the disturbing factor

of the accumulation of bile in the gall-bladder, and the variations of its amount in that viscus; so that the conditions of the experiment becomes reduced *to a measurement of the activity of the bile-secreting mechanism.*

Nearly all the observations relating to this subject have been made on the dog—that being the animal best suited for the purpose. The method resorted to by the earlier experimenters was that of continuously collecting the bile from a *permanent* biliary fistula, and observing how its amount and composition were affected by drugs. A permanent biliary fistula is established by occluding the common bile duct, and establishing a communication between the fundus of the gall-bladder and the exterior of the abdomen. When the wound in the abdominal wall has completely healed, and nothing remains but the fistulous opening into the gall-bladder, through which all the bile is necessarily discharged, a cannula is placed in the fistulous opening, and the bile collected either in a bag attached to the cannula, or in a large sponge placed in a tin box and secured to the abdomen of the animal. The difficulty of perfectly collecting the bile continuously day and night, while allowing of such freedom of movement on the part of the animal as is necessary for the maintenance of its health, is so serious that few investigators have succeeded in accomplishing the task. By this method Nasse, Kölliker and Müller, and Scott, severally made observations on a single

dog with reference to the effect of calomel on the biliary secretion. Being in some measure contradictory, the subject was in 1866 taken up by a committee, of which the late Professor Hughes Bennett was chairman and reporter. The method adopted by Scott and others was again employed, but although the committee pursued the subject in a much more elaborate manner than had been previously done, and although the research lasted two years, it must be admitted that it did not greatly advance our knowledge of the subject. The method of experimenting with *permanent* fistulæ was insufficient.

In 1873 Röhrig reopened the investigation of this subject. He observed the rate of biliary flow from *temporary* fistulæ in fasting curarised dogs before and after the injection of purgative agents into the stomach or intestine. But his results were entirely vitiated by the fact that instead of collecting the bile in a graduated measure and noting the amount secreted every fifteen minutes, he resorted to the old method of counting at intervals the drops of bile that fell from the cannula in the course of a minute or more,—a method necessarily inaccurate, which led him to conclusions some of them entirely opposed to clinical experience.

It appeared to me that the method of experimenting with *temporary* fistulæ on animals fasting and curarised was worthy of a more extensive trial, and was capable of being used in a manner

more refined, and of yielding results far more precise than had been obtained by Röhrig. Accordingly in 1874 I undertook a prolonged research on this subject, in which I was assisted by my pupils W. Vignol and Dr W. Dodds.

Method of Experiment.—All the experiments were performed on dogs. The dog was selected—(1) Because the size of its common bile duct renders it possible to introduce a cannula with an orifice sufficiently large to prevent its being blocked up by particles of inspissated mucus from the gall-bladder. (2) For the reason that its digestion resembles that of man, inasmuch as its stomach becomes empty when the process is completed. It is very different in the case of a rabbit, whose stomach is never empty. The selection of the dog proved fortunate, for the results of our experiments are in complete harmony with every perfectly ascertained fact regarding the *actions of medicinal agents on the human liver*, and prove that the *liver of this animal is affected in the same sense*—although it may not always be to the same degree—by substances that act on the human liver. All the experiments have been performed on animals of the same species, placed as nearly as possible under similar conditions; the results are fairly comparable, although it must be borne in mind that just as no two human beings can, even in their normal condition, be regarded as equally susceptible to the influence of any drug, neither can any two dogs be held to possess identical

susceptibilities. All the animals had *a full meal of lean meat* at three or four o'clock in the afternoon, and the experiment was begun between nine and ten o'clock on the following morning, so that the digestion and absorption of the food were completed, and the animal was therefore in a fasting condition. *This was an essential preliminary;* for, the secretion of bile is accelerated during the process of digestion, and had we taken the amount of bile secreted per hour during digestion as an index of the activity of the liver previous to the administration of a drug, our experiments would necessarily have been worthless. The disturbing effect of irregular muscular movements upon the biliary flow was prevented by injecting into a vein small doses of curara, repeated at intervals, when the motor paralysis which it induces became too slight. In consequence of the curara palsy, artificial respiration was had recourse to, and maintained at regular intervals throughout the whole experiment.

Chloroform was used during the preliminary operation in two cases, but the stimulation of the liver which it induced rendered the experiments worthless. On the other hand, we have abundantly proved that the doses of curara administered in the experiments have no influence on the biliary secretion, and do not interfere with the effects of hepatic stimulants. It is, therefore, an exceedingly valuable auxiliary in a research of this nature. The method of experiment we adopted was always

that of a *temporary* biliary fistula, established in the manner indicated at page 155. The wound in the abdominal wall was then carefully closed, and in all save the earliest experiments the animal was *thoroughly covered with cotton wool, in order to quickly restore it to its normal temperature;* and guided by a thermometer in the abdominal cavity, great care was taken to keep the temperature *normal,—a matter of no small importance,—for if the temperature fall several degrees, the liver secretes more slowly.* Röhrig estimated the velocity of the biliary secretion by counting the seconds that elapsed between the fall of the drops from the orifice of the tube. A single trial convinced us that this method is extremely laborious, and leads to inaccurate results, because it does not permit of continuous observation for any length of time.

Variations in secretion often occur independently of the administration of any substance, and it is impossible to estimate their significance, and make due allowance for them, unless the method of continuous collection of the bile be adopted.

Moreover, we saw that the degree of viscosity of the bile caused a variation in the size of the drops, and, therefore, in the intervals between their fall. We therefore abandoned this for the more accurate method of allowing the bile to flow into a fine cubic centimetre measure, and recording the quantity secreted every quarter of an hour. *In*

addition to constant collection of the bile, this method has the advantage of allowing us to ascertain the co-efficient of the secretion of bile, that is, the amount of bile secreted in a unit of time for every unit of the body weight of the animal. In a research of this nature it is absolutely necessary to ascertain the co-efficient of secretion, in order that a real knowledge of the activity of the liver may be obtained, and the powers of different stimulants compared. It is evident from the method of expirement that all our observations relate exclusively to the effects of substances on the *bile-secreting* mechanism. We have made no observations regarding their effects on *bile-expelling mechanism.* Nor do we intend to prosecute the latter part of the inquiry, for the question, *What substances stimulate the liver to secrete more bile? is of infinitely greater importance.*

Post-mortem examinations were made of the interior of the intestine, in order to compare the effect of a drug on the liver with its effect on the intestine.

The normal secretion of bile in a fasting curarised dog is shown in fig. 16. In that and all subsequent charts relating to this subject the numbers on the left of the woodcut indicate the amount of bile in cubic centimetres, while the numbers below the woodcut indicate the hours during which the secretion was collected; the amount of bile secreted being recorded every fifteen minutes. The dotted lines indicate the times at which

small doses of carara were injected into the jugular vein.

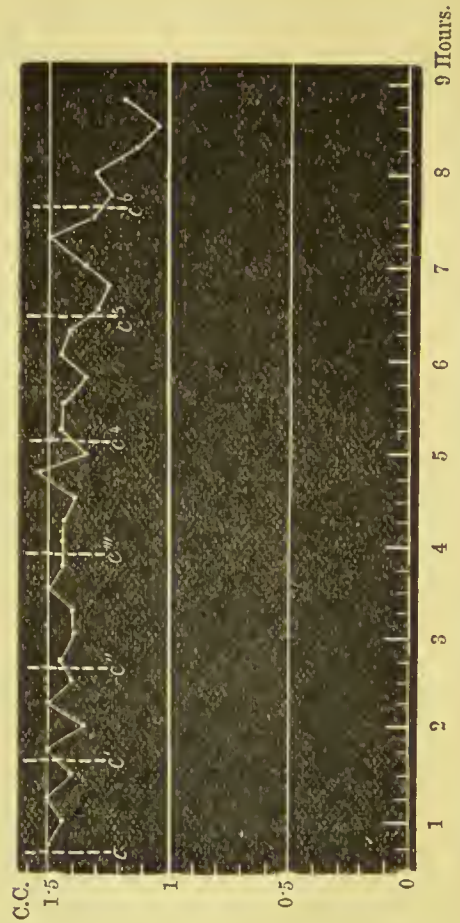


Fig. 16.—Secretion of bile by a fasting dog with nothing but curara administered. The dotted lines *c*, *c'*, and so on, indicate the injection of successive small doses of curara into jugular veins.

Fig. 16 shows a fairly constant normal secretion of bile, falling during the later hours of the experi-

ment, owing no doubt to continued want of food and consequent tendency to failure of hepatic action. The co-efficient of secretion—that is, the amount of bile secreted per hour—per kilogramme of body-weight was 0·25 c.c. In a fasting dog, when nothing but curara has been administered, the co-efficient of secretion may be as low as 0·08 c.c. It varies in different cases; 0·1 to 0·2 c.c. per hour and kilo. is a fair average.

I. *There are Substances which lower the Secretion of Bile.*—To this group belong all purely intestinal stimulants which cause a copious secretion from the intestinal glands, *e.g.*, castor oil, gamboge, sulphate of magnesia, sulphate of manganese, chloride of ammonium, &c. All the above mentioned are purely intestinal purgatives, and when their doses are considerable, they diminish the secretion of bile. They probably produce this effect in a twofold manner—(1) by draining the portal vessels; (2) by exhausting the sympathetic nervous system, and in that way influencing the liver. This lowering of bile-secretion is observed in dogs with biliary fistulæ, in which therefore no bile is allowed to enter the intestine. The effect must be more decided when a purely intestinal purgative is given under ordinary conditions, when bile is flowing into the intestine and a part of it is being reabsorbed.

A purely intestinal purgative may in some cases, however, relieve hepatic action, by removing from the intestinal canal matters which are being

absorbed into the portal vein, and which may be interfering with the due activity of the hepatic cells. In practical medicine it is important to keep in mind, that stimulation of the intestinal glands has a depressant effect on hepatic secretion.

II. *There are Substances which stimulate the Liver, but not the Intestinal Glands.*—Ipecacuan, a powerful hepatic stimulant. Increases slightly secretion of intestinal mucus, but has no other apparent effect on intestine. Maximum dose, 60 grains.

Ammonium phosphate, a powerful hepatic stimulant. Not a stimulant of intestinal glands. Dose, 5 to 20 grains.

Sodium benzoate and ammonium benzoate, both powerful hepatic stimulants. Not intestinal stimulants. Dose 10 to 20 grains.

Sodium salicylate, a powerful hepatic stimulant, but a very slight stimulant of intestinal glands. Dose, 10 to 20 grains.

Dilute nitro-hydrochloric acid, a hepatic stimulant of considerable power. Not an intestinal stimulant. Dose, 5 to 20 minims.

III. *There is a large group of Substances which are both hepatic and intestinal Stimulants.*—Some stimulate the liver more than the intestinal glands, some stimulate both powerfully, while others stimulate the intestinal glands more than the liver.

Podophyllin, a powerful stimulant of liver and intestinal glands. Dose, $\frac{1}{3}$ to 1 grain.

Iridin,—a resin from root of *Iris versicolor*,—a

powerful hepatic, but mild intestinal stimulant. Dose, 4 grains.

Euonymin,—a resin from bark of *Euonymus atropurpurcus.*—a powerful hepatic, but mild intestinal stimulant. Dose, 2 to 4 grains.

Sanguinarin,—a resin from *Sanguinaria canadensis,*—a powerful hepatic and slight intestinal stimulant. Dose, $\frac{1}{4}$ to 1 grain.

Colchicum, a stimulant of the liver and intestine. Dose, 2 grains.

Physostigma, a stimulant of liver and intestine. Dose, $\frac{1}{4}$ grain of the extract.

Phytolaccin,—a resin from root of *Phytolacca decandra,*—a powerful stimulant of liver, and feeble stimulant of intestine. Dose, 1 to 3 grains.

Hydrastin,—a resin from the root of *Hydrastis canadensis,*—a moderately powerful stimulant of liver, and feeble stimulant of intestine. Dose, 1 to 2 grains.

Baptisin,—a resin from *Baptisia tinctoria,*—a moderately powerful hepatic and intestinal stimulant. Dose, 2 to 5 grains.

Rhubarb, a mild hepatic and intestinal stimulant. Dose, 10 to 30 grains.

Leptandrin—a resin from root of *Leptandra virginica,*—a mild hepatic and intestinal stimulant. Dose, $\frac{1}{2}$ to 3 grains.

Juglandin,—a resin from root of *Juglans cinerea,*—a mild hepatic and intestinal stimulant. Dose, 2 to 5 grains.

Aloes, colocynth, jalap, all powerful intestinal stimulants, also stimulate liver.

Senna, scammony, taraxacum, scarcely at all stimulate liver. Senna and scammony are powerful intestinal stimulants.

Sodium phosphate, a powerful hepatic and moderately powerful stimulant of intestine. Dose, 120 to 480 grains.

Sodium sulphate, a powerful stimulant of intestine, moderately powerful stimulant of liver. Dose, 240 to 480 grains.

Potassium sulphate, a powerful stimulant of liver and intestine.

Rochelle salt, a powerful stimulant of intestine, feeble stimulant of liver.

Sodium chloride, a very feeble stimulant of liver, a considerable stimulant of intestinal glands.

Calomel in experiments on dog always stimulated intestinal glands powerfully, but did not stimulate the liver. Dose, 1 to 5 grains.

Mercuric chloride, a powerful stimulant of liver, but slight stimulant of intestine. Dose $\frac{1}{10}$ to $\frac{1}{4}$ grain.

IV. *There are many Substances which produce no evident effect on Bile Secretion, e.g.,* atropia, morphia, hyoscyamus, alcohol, sodium bicarbonate, potassium bicarbonate, potassium iodide.

All the foregoing statements have immediate reference to the effects of substances on the *bile-secreting mechanism* of the *dog*. The *bile-expelling mechanism* which, as regards the action of drugs, is probably far less important, was not the subject of experiment.

NOTES OF LECTURES ON PHYSIOLOGY

BY PROFESSOR RUTHERFORD.

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